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VOLUME I



## Foreword

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THERE is a growing tendency among groups of men studying different aspects of the same subject to collect and republish in one volume the results of their investigations. This practice is most helpful and it is one which will be greatly appreciated by other investigators.

The present volume of papers by associates in the Laboratory of Experimental Surgery of New York University, bearing as it does on vital subjects in scientific medicine, is a happy example of such efficient cooperative effort and one which may well be emulated by others. The contents should be familiar to every surgeon since its subject matter is representative not only of the surgery of today but of tomorrow.

WILLIAM J. MAYO.

November 18, 1915.





## INTRODUCTION

THE contents of this volume have been arranged in accordance with the newer viewpoint that surgery should deal first with the greater problems of function and diagnosis, therapeutic progress being obviously dependent upon these; and second, with the details of method and technic. This viewpoint is presented in some detail in the article on "Medicine and the World War," in which the authors discuss the growing importance of laboratories of surgical research, not alone for teaching purposes but for the furtherance of the new science of preventive surgery.

A group of papers detailing certain studies upon the alimentary and neural canals and vertebral column follows and it will be seen that biology and particularly its branches, physiological chemistry and heredity, are the underlying basis of this work.

The next group of papers upon the Abderhalden reaction chronicle a series of efforts to apply chemistry directly to surgical diagnosis; and, whatever the final deduction, these studies are in harmony with the biological era into which surgery has passed.

Following these are the details of a series of studies of the ureteral neuro-musculature, of the function of the ureterovesical valve and of an operative procedure logically based upon these functional findings. Perhaps better than any other, this series illustrates the present tendency in surgery to substitute functional for anatomical facts as a basis for new operative therapeutics; to correlate function and morphology and to place reason above technic. One might properly speak of this trend as pragmatic surgery.

The intricate subject of shock has been studied carefully and the provisional results tend to disprove some of the most widely circulated hypotheses as to its nature and origin.

Finally, technical and miscellaneous papers are grouped together.

For the information of laymen who may examine these papers, it is stated that all the experimental work herein detailed was done upon animals after complete anesthesia and that morphine has been freely used to prevent post operative pain. Physicians and surgeons, of course, understand that no operative work can be done on animals satisfactorily except under full anesthesia.

JOHN WILLIAM DRAPER, *Editor*









## ACKNOWLEDGMENT

GRATEFUL acknowledgment is made by Professor Stewart, by the Editor, Dr. John W. Draper, and by the writers of the various papers,—

To Chancellor Brown for encouragement at all stages of the work; To Dr. William J. Mayo for writing the foreword; To Professor Holmes C. Jackson for valuable suggestions and for the use of the physiological laboratory; To Professor Symmers and Dr. Fraser of the department of Pathology for technical help; To Dr. Noble of the department of Bacteriology; To Professor George B. Wallace; To Dr. Charles L. Bristol, Professor of Biology, New York University, for constant encouragement and constructive help; To Professor George Huntington of Columbia University; To Professor Charles B. Davenport of the Carnegie Institute for assistance with certain of the details relating to heredity; To Miss Jean B. Barr, Assistant Registrar of the University, for efficient aid in making this volume.

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## MEDICINE AND THE WORLD WAR

### Surgery and the New Degrees in Science and Philosophy— A New Era in Teaching and in Hospital Management<sup>1</sup>

BY GEORGE DAVID STEWART AND JOHN WILLIAM DRAPER,  
New York.

For many years, if not permanently, the devastation of Europe will place progressive medicine in the hands of America. This change would have come soon owing to the material and intellectual resources of our continent and to the cosmopolitan character of our citizens; but the great war has achieved in a day what would normally have taken years, and has thrust upon this country the duty of fostering the growth, uprooted and ruined in Europe, of that great science which, above all others, holds out hope to man and points the way to a future and truer civilization.

With the science of medicine constantly changing and enlarging, the task of teaching, always behind the science, becomes yearly more tremendous, and curricula are more and more overloaded. The writers, realizing the impossibility of giving consideration to the whole subject, wish to direct attention particularly to surgery and manifestly to only a few phases in the development and the teaching of this science, pointing out that if progress is to be made the growth of the two should go hand in hand. For, no matter how far we advance the science, if not taught to our successors, progress will be arrested. With our accustomed load of responsibilities and the added ones which have been thrust upon us by the world calamity each new step is fraught with additional responsibilities. That we are not alone in holding this pessimistic point of view is attested by such opinions as that of the historian Eduard Meyer (quoted by Russell, *Atlantic Monthly*, July 15, 1915), who considers Germany as the analogue of Rome and England as the analogue of Carthage, and looks forward to a succession of conflicts like the Punic wars.

The essayists wish to consider the following general topics: (1) hospital intern systems, and teaching as it now exists, particularly in the east, with some suggestions

<sup>1</sup>Paper read before the American Hospital Association, San Francisco, June 22-25, 1915. From the Department of Surgery, New York University.

it is essential to the development of surgeons and to the cultivation of their individuality.

#### A POSSIBLE SCHEDULE

The time that it will take to make a surgeon, and the methods employed, are bound to vary, depending somewhat on conditions, somewhat on the man. The main thing is to set up and maintain a standard uniform enough to produce good workers without destroying individuality.

Bernays says, "After graduation the student must become attached to a hospital or he must become assistant to a hospital surgeon so that he may take part in the daily exercise of the science and art of surgery. Exactly how many years should thus be spent, I cannot say; one, two, or three years should suffice to turn out a surgeon who is capable and ready to offer his services to the public with a good prospect of making a useful and successful diagnostitian and operator, after the completion of further study."

Allen says, in discussing this subject: "First, thorough and broad instruction; second, prolonged hospital residence and post-graduate study; and third, the establishment of some standard of attainment which must be reached by men to gain their general recognition by the profession. If these ends be attained, the community and the general profession will not long remain in doubt as to the men who are deserving of their confidence and support. Such a standard would do much to protect the public from incompetent men, and to place in the hands of capable surgeons those facilities which they alone are able to utilize to the best development of their profession, and the best interests of humanity."

The plan of hospital reorganization that the essayists wish to suggest contemplates a short hospital training for all men (one year), longer training for the better men (promotion within the ranks), and, finally, remuneration after men have been in service for a certain length of time.

In order to give all graduates the advantage of the hospital it will be necessary, for some time at least, to shorten the time of hospital training to one year for the rank and file of men—which practically amounts to adding one year to the four years' course in medicine as now given, a step long favored by many educators. To make better trained men, however, it is proposed that the abler ones be given additional opportunities, so that at the year's end they may be offered advancement, the promotion being based

on examination and knowledge of their capacity, character, and achievement, in part, at least in creative work. This amounts to promotion within the ranks and should be based strictly on merit, determined by fitness. At present, when a student after graduation selects surgery, he will continue in surgery, no matter how unfitted he may turn out to be; and at the end of two years he will consider himself a surgeon and be willing for a consideration to offer his services to anybody. By the method of promotion within the ranks, if he has not the capacity to become a surgeon, he will be dropped at the end of his first year. The knowledge that a few of their number at the end of the first year will receive promotion, and that a still smaller number may be appointed to positions as residents at the end of the second year, will keep alive a constant striving and ambition, and bring out the best that is in each one. This has recently been offered by one of the writers for adoption as the basis for the intern system of Bellevue Hospital.

This compulsory hospital year, with a preliminary compulsory academic year following high school added to the usual four years' course, will amount to a six-year course in medicine, and it is believed by the essayists that this offers a better disposition of the time than to compel men to possess an academic degree preliminary to the study of medicine; at least, until much of the useless matter now taught in the academic as well as in the medical schools is abolished, making room for more profitable work.

To amplify, it is believed that under existing conditions, one year of special preparation following high school, and one year of hospital training following graduation, are of more value to many men than the four years spent in acquiring an academic degree. After all, the fact is that we are dealing with the average man who is going to practice among his average fellows, and there is such a thing as over-training in medicine, with consequent loss of initiative and efficiency.

It must have been observed by all educators that the ordinary human mind is capable of acquiring a certain amount of knowledge, and after this has been stored, the limits of capacity have been attained, and the owner, if pushed, becomes stale. This accounts for the phenomenon that often presents itself when a student, possessing an academic degree, is outdistanced by one who holds only a high school diploma, but is able to keep up steam all through his medical course. Heredity, no doubt, has as

much to do with these phenomena as environment, but the one is immutable while the other is subject to modification. Take such a man of the rank and file, gone stale—take him from the task of acquiring, give him applied work; close his books, for the time at least, and under the stimulus of his environment and problems he will develop again along other and useful lines. How helpful it would be if a feasible index or measure of a student's real limitations and capacities could be found! Such a scale is as necessary to medical education as it is to commerce and the mechanical arts, where it has long been sought. We shall hail with delight the medical efficiency engineer.

It will be argued that such a schedule would take a great deal of time, but it must be observed that it is capable of infinite variety and, depending on his fitness and ambitions, the young man may drop out at the end of any one-year period or at the close of the whole period. If he stays through and is fit, he ought to and likely will be promoted in the service of the hospital and university.

In the case of those whose service is long, it is believed that some form of payment should be arranged for each year after the first, and certainly after the second year of service. Indeed, it is to be expected that when the public, represented particularly by the lay hospital boards, awakens to the vast economic principles involved here (for every day the sociologic side of hospital work becomes clearer to all) they will be willing to pay even the interns. It is at this time that the average man, having spent all his family can afford, needs to earn at least money enough to support him, and it is believed that under some such plan he may receive fully as much as is collected on the average by the beginner in embryonic and essentially unproductive practice.

No doubt many other schedules will be suggested to fit special environments, but as we have already stated, the important thing is to make a beginning.

The development of the science under the continental system depended, as has been stated by a surgeon, upon amazing patience in pursuing long courses, upon accurate knowledge of anatomy, upon familiarity with gross pathology, willingness to serve long apprenticeships, and a devotion to a life with but small compensation. It might be and is urged in opposition to the continued success of these methods that there is a rather noteworthy and widespread lack of the application of the laws of physiology to continental surgery and that a long period spent as



assistant is almost certain to repress initiative and to subordinate individuality.

Certain it is that the impression gained by an American surgeon visiting the continental surgical clinics, aside from the marked contrast in the handling of the individual patients, is the difference in technical skill. Good dissectors are common, but surgeons are not longer bred in the dead-house. Rare, indeed, is the American surgeon who would choose to be operated on on the continent in preference to America! The poorer technic and the persistence on the continent of the pathological era in surgery are the two important sign posts which pointed to the early transfer of surgical progress to America long before the war.

Even admitting its value, it may not be concluded that we can transplant these methods to American soil any more than make student duels popular. Before the transplant could grow the entire environment would have to be changed. For instance, there the youthful doctor receives respect and has opportunity, and his small salary is sufficient; here, without a practice, he finds little comfort in watching a broker or manufacturer who has a five-thousand-dollar limousine and a box at the opera, both of which may be denied to himself for his entire professional career. Nor is the time urged in any of these schedules long as compared to that of the practitioner of Parés time, who lived in the house of the master for two years in Paris and then followed the Spanish army in the low countries for four years longer to see whether the Italians or Germans or Spanish had any advantage over the modest Ambrose, who wrote: "I have certainly touched the mark whereat I aimed so that antiquity may seem to have nothing left wherein it may exceed us besides the glory of invention, nor posterity anything left but a certain hope to add some things, as it is easy to add to former inventions."

Such is a review of the well known system of hospital training generally received by the young surgeon. In brief, he is taught a highly technical therapy out of all proportion to the training given in diagnosis. We do not mean to imply by this that the training of the young physician is one whit better, for it is at least equally lacking; but we are here particularly concerned, as already stated, with the student who is to become a surgeon. Because of the greater damage and of the greater good he can do, it is well to improve his standing first.

Turning now to the second point under consideration, it is a certain prediction that the best results in the future will be largely a matter of team work. Medicine is too complex for any one man to attain a complete understanding of any considerable part. In the old days, a student went into the house of the master, who became his preceptor. Ordinarily, their reciprocal relations were not of much advantage to either. The preceptor told stories and the student compounded Gregory mixtures. Today we believe that after graduation the student, now a doctor, should become closely allied with older and busier men. It is easy to see that the benefits are not by any means one-sided and that added ones should accrue to both or to all the members of this medical partnership. Indeed, the first thing that strikes one is the value of that free discussion and consultation which takes place without added expense to the patient.

Who would think today, as Ochsner well says, of attempting to operate a shoe factory by the methods of fifty years ago? That is what many hospitals and physicians are still trying to do; no wonder they are outstripped by institutions and men using modern equipments! Thus has come about the medical corporation—best developed in the west and for the time, at least, answering admirably the intricate requirements of present-day medicine.

If today calls for corporate medicine, communal medicine may be the method of tomorrow. Mention has been made on the one hand of the quasi-public nature of our profession, of the direct and vital interest in it which every layman has or ought to have; of the complexity of our problems, the impossibility of any one man being able to solve or even to grasp them all; and of the expense, on the other hand, of submitting them to a group of specialists; of the necessity on this account for team work; of treatment by companies of physicians or by hospital staffs. All of these tend to make treatment, at least preventive treatment, a matter of *institutional* care. This has been done here and elsewhere by boards of health, and in England under the insurance act; a large part of the medical profession have become public servants and are paid for their public work out of the public treasury.

Discussing the possibility of medicine becoming institutional in the future, particularly preventive medicine, the retiring medical officer of the New York State Board, in a recent interview, has pointed out the tendency in this direction, but has refrained from predictions.

In passing, he states that it is believed that under the Lloyd George Insurance Act much of the medical service rendered is perfunctory, and cites the further danger that doctors may lose initiative. As to the possibility that this will come about, one can at present only class the act with the referendum and recall, or rather, with government ownership of railways and telephones. So far as we know, these are still *sub judice*; to make them a success, the whole order of the world will have to undergo readjustment. The essayists are far from believing, however, that such readjustment may not come or, indeed, that it may not already be close at hand. In any event, they stand uncompromisingly for the preservation of individuality even at some loss of efficiency.

Turning from the hospital intern system and corporate medicine to the surgical training of the universities, it is timely to inquire as to what factor has been at work in causing the universities to admit their departments of surgery to their graduate schools. It is because the university has recognized in the laboratory of physiological, surgical research a factor of great educational value and the link between applied surgery and the natural sciences.

Laboratory methods in teaching surgery to undergraduates were first shown to be of permanent value about fifteen years ago. Surgery is indebted to W. S. Halsted for the stabilizing of this innovation, and the present position of the laboratory unit in departmental work is due primarily to the genius for teaching of this far-sighted man.

Halsted's ability for training men is second only to his capacity for surgical research, and he early discerned that the surgical laboratory in the hands of the head of a department of surgery would be an invaluable tool for evolving new surgical facts and creating a new race of surgeons whose viewpoint would be philosophical rather than technical.

Since then the rapidity of the growth of the surgical laboratory in our leading universities has been truly amazing, each prominent medical school being now more or less thoroughly equipped with the mechanical requirement for such a unit. The laboratory has become an integral permanent division of each surgical department, and as in all cases where growth has outstripped adaptation, the material equipment having outgrown the academic application, it may be well to pause and to consider some of the pressing problems which have thus arisen. Prominent

among these are, what should be taught, to whom it should be taught, and the time which should be devoted to the course. Fixed must be the growing conviction that the surgical laboratory staff, to accomplish the best results, must be given full hospital facilities, together with recognition and promotion for achievement at the same rate at which it is now given men who work only in the dispensary and the wards. This will come with further enlightenment. The necessary hospital readjustments which are inevitable as the graduate surgical student takes his place in the wards, are likewise subjects for thought and action. For the advent of such workers, whose advanced degrees will be won as much in the wards as in the laboratory, together with the application of a system such as proposed, will mark the passing of the merely technical intern. By the system of rotation proposed, the surgical residents will become medical academicians first and technicians afterwards. We can depend upon the laboratory to break the evil and antiquated conception of a distinction between medicine and surgery, and to give a new and pragmatic viewpoint.

The problem of coordinating the workers and of interlocking their results is by no means an easy one, but a correlation of the hospital ward, the dispensary and the surgical laboratory for undergraduate and graduate teaching and for hospital welfare alike is necessary. In the earlier day, not by any means remote, this was a simple matter, for the granting of clinical opportunity in the hospital and promotion of the teaching staff went along hand in hand almost automatically. One factor tending to simplify conditions of these earlier days was that surgery was very justly considered by the university authorities as a technical art, quite outside of the academic pale, nor could any one justly assert, however partial he might have been to that art, that the academicians were incorrect in their viewpoint. Now, however, the universities have begun to admit their departments of surgery into their graduate schools on the same basis as physiology and anatomy, granting the usual advanced degrees in science or philosophy for the study of surgical problems; and such degrees will be granted for the studies upon the human as well as upon the lower vertebrate body, the whole question being obviously one of comparative mammalian pathological physiology. Departmental heads, therefore, must promptly recognize that the old barrier between so-called "practical" and "theoretical" workers in surgery was a



bad one. This position has just been taken by New York University. It must give place to the modern conception that laboratory training, with its logic, its inductive and deductive philosophy, far from unfitting men for the work of applied surgery, certainly equips them for the best and most progressive constructive work. The writers of this article wish to make it clear that they consider bedside work essential, but that no amount of it can ever take the place of laboratory training in the making of a surgeon, the one being complementary to the other. The teachers of the greatest post-graduate school in the world, the Mayo Clinic, hold that the operative technic is the last to be considered and the fundamentals of diagnosis the first, and with them we heartily agree. Diagnosis has its roots deep in bio-chemistry and physiology. The profession looks to the hospitals in no less degree than to the medical schools to support and give proper advancement in the wards to young men who elect to spend a large part of their post-graduate time in the study of these sciences. Otherwise, if preference is given to men who simply do ward work, men who seek hospital services will fear to give requisite attention to research.

The following quotations from Deaver (Deaver and Pfeiffer, *L. I. Med. Jour.* July, 1915) serve well to indicate the trend of modern surgical thought:

"If a medical school can produce graduates who think correctly and advise wisely in surgical diseases it will have accomplished its proper task. The development of surgical sense, of a correct understanding of the role of surgery in prevention and cure, should be the aim of instruction; methods, procedures and handicraft are secondary considerations."

"The best book on surgery is the latest work on physiology."

"The mere craftsman is no longer entitled to be called a surgeon; he must be a biologist, bacteriologist, and pathologist. Any course in surgery which does not prominently recognize the changed relations between the head and hand of the surgeon is not modern and is not satisfactory."

It is our impression that the modern department of surgery must consist of three closely correlated divisions, to-wit:

1. Applied or therapeutic surgery.
2. Diagnostic or deductive surgery.
3. Experimental or inductive surgery.

These three are not named in order of relative importance, but in order of their evolution. It seems not improbable that when arranged in accordance with their true value this order will be reversed. Such a rearrangement would lead the student through induction, from simple experimentation to deduction or diagnosis, and finally, to the applied or therapeutic side of the knowledge. The deduc-

tive method is obviously fitted to the mature mind of wide experience; the inductive is essentially the method of the young mind, with little or no experience.

We agree with Jonas, who says that principles, rather than technic, should be taught in surgical laboratories; and this conclusion is based upon our fourteen years of experience in surgical laboratory teaching. We are convinced that much evil may result from routine teaching of operative technic, for one of the objections to today's training is that technic has been made too easy. Is not this the lament of every well trained surgeon who is obliged to spend a large part of his time in repairing the damage done by technicians who, unfortunately for the patient, were nothing more than mere craftsmen? Such lacerations are not longer to be confounded with operations based on physiology, however cleverly they may be executed, for they give bad results and discredit surgery. Undergraduate technic should be learned chiefly in the minor surgery, in bacteriology and upon the human cadaver. The surgical laboratory should be open to the senior students only and to those in whom the scientific mind is coupled with manual skill. Just what the post-graduate laboratory teaching should be is still, as intimated, a matter of doubt, but the following outline has proven serviceable. Its best use, perhaps, is to illustrate that more and more surgery is coming under the domain of law, and thus amply to justify its acceptance by the graduate schools of philosophy. As has been written:

"All mundane events are the results of operation of law. Every movement in the skies or upon the earth proclaims to us that the universe is under government.

"Physiology, in its progress, has passed through the same phases as physics. Living beings have been considered as beyond the power of external influences, and, conspicuously among them, man has been affirmed to be independent of the forces that rule the world in which he lives." Draper's Intellectual Development of Europe.

Modern surgery concedes man's dependence upon these forces and insists that no therapy can possibly avail unless based upon them.

#### A. Alimentary tract.

1. The dynamics of the alimentary canal. Dilatation, stricture, ulceration, tetany, atony, autonomic relations, heredity.

2. Internal secretions of the duodenum in relation to death from intestinal obstruction and auto-intoxications.

3. Law of organic compensation in special relation to surgical therapeutics, ablation and the post-operative readjustments of the organism, ileostomy and the vicarious assumption of colonic function. Colectomy, gastrectomy.



## B. Urinary tract.

1. Dynamics of the ureter and bladder. Dilatation and law of compensation. Stricture, neuro-muscular impairment.

2. Paramount importance of the ureteral prostalsis over the uretero-vesical valve. Hydronephrosis and renal infection.

3. Surgical analogy between the alimentary and urinary neuro-muscular tubes and valves.

4. Uretero-enteric anastomosis based on surgical physiology.

## C. Cerebro-spinal system.

1. Hyperthermia in connection with decompression.

2. Experimental studies in increased intradural pressure, concussion, contusion, etc. Experimental optic neuritis.

3. Experimental spina bifida. Relation of heredity.

The admission of surgery to academic university standing is a step of great importance, not alone in itself but in the opportunity which it creates for the hospitals to increase the number and quality of ward workers. The essayists feel that this departure may be the vantage ground of many new lines of thought and action.

The distinction between medicine and surgery has faded almost entirely away, and with it the old idea that the "practical" man, whatever that meant, was superior in applied work to the so-called "theoretical" man, who might decide to turn his attention in part to applied surgery. Laboratory studies must be put on equal footing with ward work in hospital recognition and advancement.

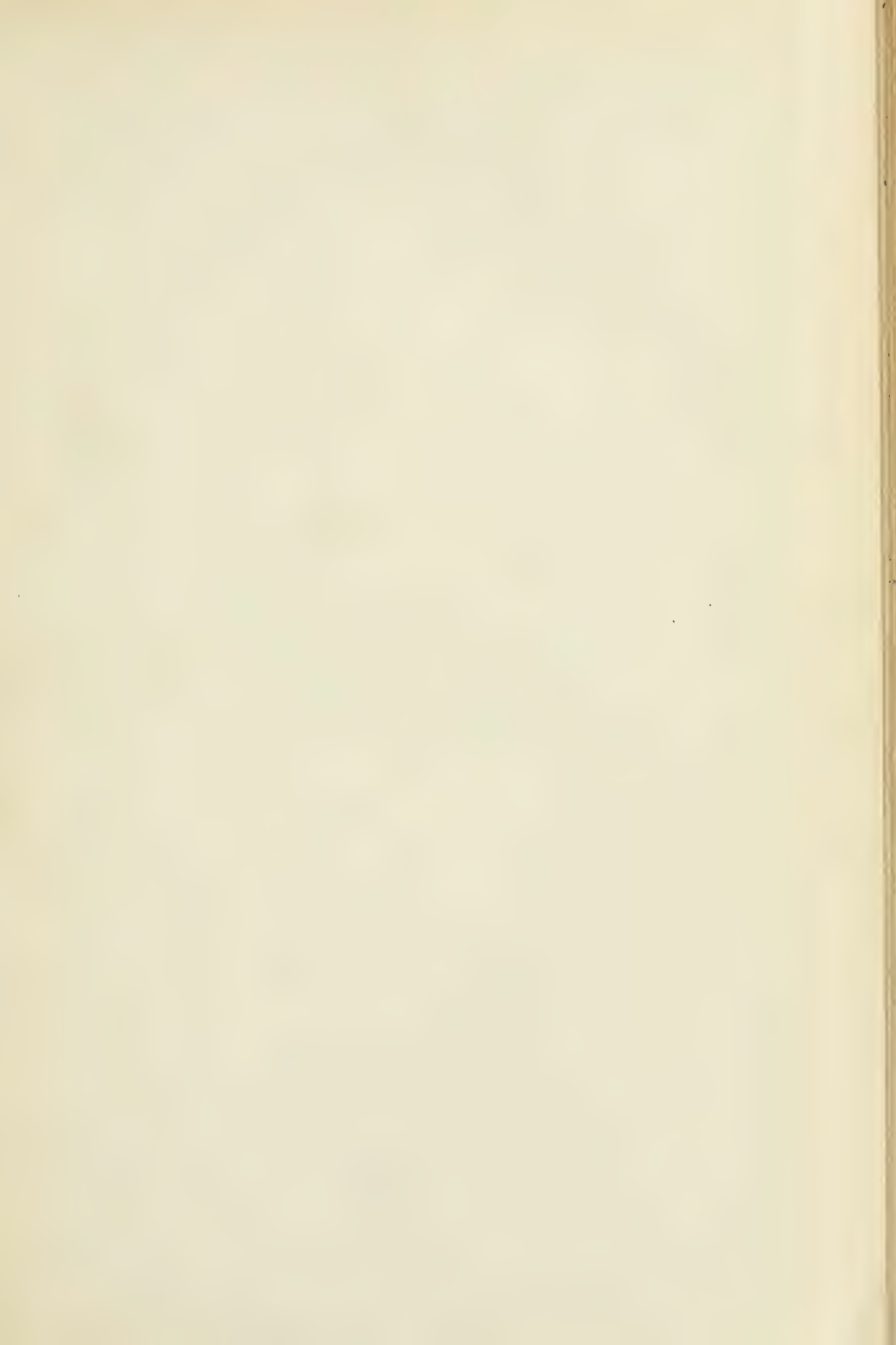
Hospital services should be mixed, but the mixture must be constant, not alternating. Medical and surgical wards should be much more closely identified and all petty strife between the services eliminated. It is also believed that the time will soon come when the so-called medical man will visit the surgical wards, and the surgeon be made welcome by his medical confrere at the bedside of patients who may in no sense require operation.

Indeed, if one considers the frequency with which the operating doctor visits and inspects the cavities of his patients, there to see the living pathology rather than terminal dead house conditions, it could in no wise be considered unjust if one applied to the surgeon, rather than to the physician, the term of internist—iconoclastic, perhaps, but true.

All new hospital cases should be admitted to a diagnosis

ward for impartial study. It is absurd that sectarianism should longer be tolerated in medicine, in view of the healthy pragmatism which is rapidly replacing the dogmatism of the past, and of the broad and generous viewpoint with which medicine and surgery have recently been endowed because of their acceptance of scientific truth.

Full recognition by the graduate schools and a free hand to correlate surgical studies upon lower mammals with coordinate studies upon the highest mammal, man, in the surgical laboratories and in the hospital wards, will tend further to fuse medicine and surgery, improve the grade of students, diffuse knowledge, and ultimately serve to lighten the burden of fostering medical progress which has suddenly come to America because of the great war.





# STUDIES IN INTESTINAL OBSTRUCTION

WITH A REPORT OF FEEDING HETEROLOGOUS  
JEJUNAL AND ILEAC CELLS TO A  
HUMAN BEING \*

JOHN WILLIAM DRAPER, M.D.

NEW YORK

To Roger we are indebted for the present conception of the cause of death in intestinal obstruction. He was undoubtedly the first to conceive of it as a true auto-intoxication.

In a paper read before the Johns Hopkins Medical Society seven years ago and based on a study of the effects of 400 duodenal obstructions produced in animals at the Surgical Research Laboratory at Columbia, I reported corroborative evidence, from a surgical aspect, of Roger's view. William Welch on opening the discussion of my paper said that, if corroborated, the facts presented would show that the duodenum had a function hitherto unknown and one evidently of the utmost importance in medicine. It is gratifying that this corroboration has just recently come from Dr. Welch's own laboratory at the hands of Whipple and his associates. By a series of skillfully devised experiments, these investigators have succeeded in casting much more light on this interesting problem than either Roger or I had been able to do, and the sum of our investigations taken in the aggregate seems now to offer incontrovertible proof that the cause of death is not bacterial in origin but truly autotoxic from the cells of the epithelium of the intestine itself.

Perhaps no branch of medical research better illustrates than this one the advantages derived from having men with one object in view working at different

\* From the Laboratory of Experimental Surgery, New York University.

\* Read before the Section on Pathology and Physiology at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

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centers of education toward the solution of a common problem. The different points of view ultimately arrange themselves on convergent lines so that when the answer is finally won it is evidently not the product of one man's aims or ambitions, but a homogeneous unit, resulting from the constructive work of several minds. For no single individual can expect to do much more with a modern problem than to advance it a single step. This problem also serves to demonstrate the rapid breaking down of the traditional barriers between medicine and surgery, forecasting the ultimate fusion of these old and arbitrary subdivisions into a new unit, the members of which will have a working knowledge of physiologic chemistry and its allied sciences in addition to requisite technical skill. Furthermore, it demonstrates that modern surgery, like physiology, does not consist in the manufacture and use of instruments of mechanical precision but in philosophical interpretation of natural phenomena.

The various old and groundless theories as to the cause of death in intestinal obstruction have one by one been disposed of, with the possible exception of the exact origin of the toxemia. Is it bacterial, or purely autotoxic from the cells of the intestinal epithelium itself? Were it not for the views of Fred Murphy, which result from his studies at the Washington University and which bear evidence favorable to the bacterial theory, one would be ready to accept the result of the painstaking and thorough researches at the Cornell laboratories of Hartwell and Hoguet who seem definitely to have excluded the anaerobes, and of Whipple and his associates at the Hopkins laboratories, who are disposed to rule out all bacteria as causative agents in the development of the toxemia. From the prosaic and common sense point of view of applied surgery, it is hard to understand why obstruction in the duodenal region should be many times as dangerous as obstruction in the colon. It has long been known that duodenal contents may be allowed to escape into the peritoneal cavity without danger, but that peritonitis is to be expected if any colonic contents escape.

No careful observer could watch the death of a series of duodenally obstructed dogs without noticing the close similarity between the ante-mortem symp-



toms of this condition and those seen after parathyroidectomy or long remain in doubt that the function of the liver was greatly impaired in each.

The accompanying tables are based on the study of the urine of duodenally obstructed dogs, both before and after a large dose of camphor had been given hypodermatically. The recovery of the paired glycuronic camphor has been made by the method devised by Tollens. I am indebted to Frederick W. Schlutz of the University of Minnesota for the privilege of presenting these results, which are a chronicle of his chemical studies made on dogs obstructed by me. In a previous communication we have jointly presented two similar studies, both of which appear to show more conclusively than the present ones that

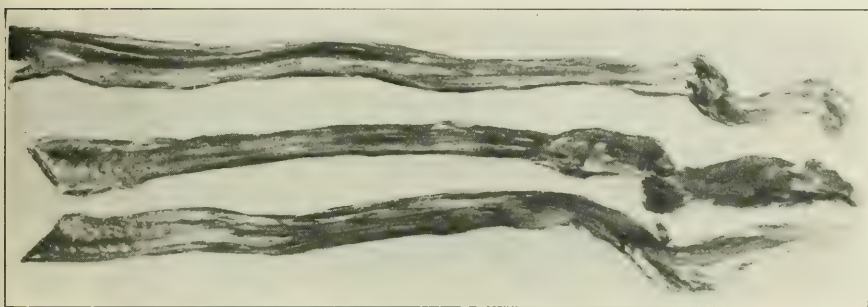


Fig. 1.—Above, the split colon of a normal dog; in the middle, the split colon of a dog salivated for four days by pilocarpin, and below the split colon of a dog dying from acute duodenal obstruction.

liver function was impaired. Negative findings, reported of carefully wrought work, are, however, just as valuable as positive findings, particularly in the case of a method which is as yet open to some question as to accuracy, and which is certainly open to criticism as regards the time taken in working it out. Dr. Schlutz is carrying on further studies of the accuracy of Tollens' method. As indicated in Table 1, the discrepancy between this report and our previous findings, in which the liver function, as indicated in terms of camphor-glycuronic was considerably lowered, may be due either to inaccuracies in the method itself or our application of it, or to the fact that we were unfortunate in having one of our dogs

live but a very short time while the other one lived an unusually long time. Dr. Schlutz will make a further report which will clarify this interesting question.

When Hartwell and Hoguet advanced their hypothesis that water privation was the chief lethal factor after intestinal obstruction, at the suggestion and with the help of George Wallace we conducted some experiments to determine the exact water percentages in the tissue of dogs under various conditions. It was thought that salivation by pilocarpin, fasting, and duodenal obstruction might cause approximately the same water-loss to the tissues.

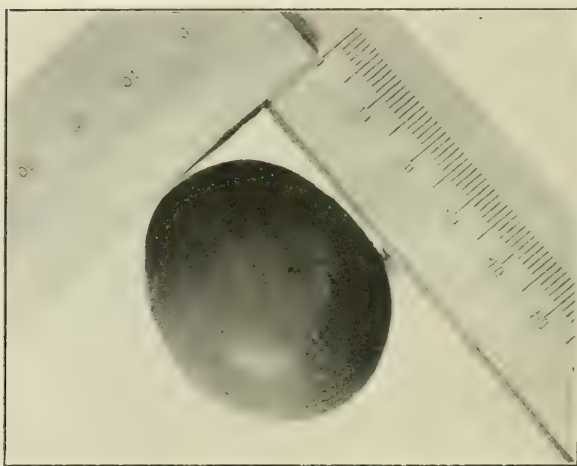


Fig. 2.—Acute jejunal obstruction in dog. Stone swallowed six months before operation, causing chronic stomach symptoms, but no obstruction until it slipped into the bowel. Note partial digestion of soft area by gastric juice. Recovery followed removal of pebble and feeding of dog with jejunal and ileac epithelium.

Table 3 shows the results from six tissues, namely, liver, lung, heart, kidney, spleen and muscle. It is seen that within a few tenths of 1 per cent. the water-loss after pilocarpin, after fasting, and after death from duodenal obstruction was the same, namely, 10 per cent. In the case of the salivated dogs and the fasting dogs, euthanasia was practiced on the fourth and seventh day, respectively, long before there were any signs of disability. On the other

hand, the duodenally obstructed dogs were allowed to die of their autotoxemia, so Table 3 gives the maximum water-loss for obstruction but not for salivation or for fasting.

These studies appear to offer additional proof that in intestinal-obstruction toxemia, as in other toxemias, whether bacterial or truly autotoxic in origin, the

TABLE 1.—INTESTINAL OBSTRUCTION, DOG 201: LIVER FUNCTION IN TERMS OF GLYCURONIC CAMPHOR (TOLLENS), SCHLUTZ-DRAPER SERIES

Date of Experiment	Length of Period, Hrs.	Vol. of Urine, c.c.	Normal Amt. of Glycuronic Acid	Amt. actually Passed as Combined Camphor Glyc. Acid	Increase Over Normal in Glycur.	Remarks
1-27-28	24	130	0.1794	.....	.....	2 gm. of camphor.
1-28-29	24	122	0.1092	.....	.....	A Theoret. total of 452 gm. Comb. camph. glyc. acid. 37.02 per cent. combined before, 5.64 per cent. obstruction.
						Camphor 2 gm. hypod. 3 p. m.
1-29-30	24	147	0.1470	0.4428	0.2958	1 c.c. of normal undiluted urine = 0.0010 gm. glyc. acid.
1-30-31	24	215	0.2150	1.4094	1.1944	1 c.c. of normal diluted urine = 0.00028 gm. glyc. acid.
1-30-11-1	25	227	0.2270	0.4104	0.1834	Intestinal obstruction, 3 p. m. 7-1912; 24 hrs. later 1 gm. camphor hypodermically.
11-1-2	34	900	0.9200	1.1772	0.2572	

Discrepancy with results previously reported may be due to short post operative life or to inaccuracy of Tollens' method.

solvent power of water on the toxins and its help in eliminating them from the body serve in many cases to prolong life, and, under certain conditions, to save it. Indeed, Wallace has shown that an animal may be given double the lethal dose of diphtheria toxin and yet live, if treated by abundant hypodermoclysis. But while valuable from a therapeutic point of view they cast no light whatever on the

origin or the nature of the toxins. Furthermore, it has been the clinical experience of all surgeons that even an abundance of water will not serve to save the life of a human being in whom there had existed for any length of time complete duodenal obstruction.

We have again subjected to careful microscopic study the liver, heart and kidneys of a large number of obstructed animals and find that except for capillary dilatation they appear normal. In this connection as well as in the conduction of the feeding experiments, I acknowledge the efficient help of Dr. Eisberg. These microscopic findings are simply corroborative of previous reports made by myself and others. The beginning and end of the alimentary canal, however, on its epithelial surface, shows this capillary dilatation so markedly as to attract the eye on gross examination. I have shown a colored photograph of a stomach removed from a duodenally obstructed dog at the Mayo Clinic. I have shown and called attention to this before, without knowing its importance or significance; and because of its bearing on certain data which I shall present later, I am glad to say that the observation is corroborated by Whipple. In our necropsy experience the small intestine has shown little if any, gross change, but the colon is almost invariably affected and in a very characteristic manner. I understand from Wallace that the same condition obtained after a lethal dose of diphtheria toxin had been given.

Thus it appears increasingly probable that the toxins of intestinal obstruction are eliminated both from the stomach and from the colon. When we recall the method of elimination by the stomach of morphin, its reabsorption by that organ and the value of frequent stomach-washings in the treatment of morphin poisoning, the post-mortem picture of intestinal obstruction is not so surprising, and the value of lavage and epithelial cell feeding in complete and incomplete obstruction as well as in acute dilatation of the stomach is more easily understood. It strongly suggests that most cases of postoperative dilatation are due to an adynamic duodenum, just as hydro-nephrotic dilatation of the kidney is often caused by physiologic ureteric obstruction. An organ dilates first at the point of obstruction to its outlet, be the obstruction mechanical or physiologic.

The capillary evidence of stomach elimination affords a working hypothesis on which we may explain the interesting results of feeding to duodenally obstructed animals the epithelial cells from the

TABLE 2.—INTESTINAL OBSTRUCTION, DOG 202: LIVER FUNCTION IN TERMS OF GLYCURONIC CAMPHOR (TOLLENS), SCHLUTZ-DRAPER SERIES

Date of Experiment	Length of Period, Hrs.	Vol. of Urine, c.c.	Normal Amt. of Glycuronic Acid	Amt. actually Passed as Combined Camphor Glyc. Acid	Increase Over Normal in Glycur.	Remarks
1-27-28	24	116	0.1458	.....	.....	1.7 gm. camphor = a theoret. total of 3.842 gm. = comb. camph. and glyc. acid. 0.2 gm. camphor = 452 gm. comb. camphor and glyc. acid.
1-28-29	24	150	0.1548	.....	.....	
1-29-30	24	83	0.0913	1.2294	1.1381	Before obstruc. 44.56 per cent. of camphor comb. with glyc. acid. After obstruc. 47.64 per cent. were comb., but practically all in the first 24 hrs. after that markedly dim. function.
1-30-31	24	100	0.1100	0.3582	0.2482	
1-31-2-1	24	130	0.1430	0.2880	0.1450	1 c.c. of normal undiluted urine = 0.0011 gm. glyc. acid.
Intestinal obstruction 4:30 p. m. 2/1/12						
2-1-2	24	55	0.0615	0.2424	0.1809	
Camphor 2 gm. subcut. 2/2/12, 2 p. m.						
2-2-3	24	366	0.4026	2.3100	1.9074	
2-3-4	24	109	0.1199	0.2310	0.1111	
2-4-5	24	246	0.2706	0.2906	0.0200	
2-5-6	24	134	0.1474	0.2208	0.0724	
2-6-7	24	85	0.0935	0.1140	0.0205	
2-7-8	24	60	0.0660	0.0888	0.0228	

Postoperative life unusually long may indicate high liver resistance or inaccuracy in Tollens' method.

ileum and jejunum of other animals. Table 4 shows the result, as regards the length of life, to be quite definite, the fed dogs living nearly twice as long as the controls. This series agrees with a similar series

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reported by me from the Mayo Clinic. It is not to be forgotten that scrapings from the frog's duodenum will stimulate pancreatic secretion in the higher vertebrates. Intercellular reactions must be among the most ancient and most fixed of our functions, and the feeding of intestinal cells may prolong life by reestablishing certain vital intercellular reactions which the obstruction had interrupted. Although knowing empirically that if jejunal and ileac epithelium were placed in the stomach of a duodenally obstructed dog, that dog would outlive one either not fed on cells at all or fed on cells of organs other than the small intestine. I could not previously understand this but it now seems probable that since the toxins are undoubtedly thrown out into the stomach they are directly rendered harmless by the heterologous cells from the small bowel derived from a healthy animal and are thus prevented from reentering the body. This explains the immediate benefits derived in the treatment of acute dilatation of the stomach and since this condition is undoubtedly due to physiologic duodenal obstruction, it seems probable that the feedings of these epithelial cells may prove to be just as useful in the treatment of dilatation as in the postoperative treatment of obstruction.

The study of Table 4, constructed from the last series, shows that it differs from the former series in that the pulse-rate of the different groups has been unaltered. A reasonable explanation of this is that the pulse was taken in the recent series at the femoral, whereas in the series reported from Rochester it was in each case taken at the apex. The femoral count is certain to be much lower when the heart is running high because many of the beats are not transmitted to the finger. While this series for the foregoing reason shows little change in the pulse-rate, it does show a much greater increase in the length of life, and this certainly is the best index of the effect of any treatment.

A glance at Table 4 shows that of the dogs fed with epithelium only two died before the hundredth hour, whereas of the controls only three lived beyond the hundredth hour. It is interesting to note that one of these lived 239 hours, showing that occasionally one finds an animal naturally resistant to duodenal obstruction. In the average this is balanced in the

TABLE 3.—WATER PERCENTAGES OF SALIVATED AND DUODENALLY OBSTRUCTED DOGS ACCORDING TO TISSUE; SALIVATED SERIES, EUTHANASIA FOURTH DAY; FASTING, EUTHANASIA SEVENTH DAY; OBSTRUCTION SERIES, AUTOTONIC DEATH ON FOURTH DAY (AVERAGE)

Tissue	Normal				Salivated (Phloccarpin)		Fasting 7 Days		Duodenally Obstructed	
	Dog	211	193	Aver.	205	Aver.	204	207	206	Aver.
Liver..	73.6	72.0	70.0	73.7	74.8	67.4	62.6	59.0	60.6	71.0
Lung..	80.4	84.3	77.6	77.6	71.2	75.1	76.8	72.8	66.8	69.8
Heart..	77.0	77.0	84.0	78.2	73.0	68.0	74.8	74.4	62.0	77.0
Kidney.	....	78.7	80.0	79.4	75.2	73.2	70.9	67.2	59.3	68.7
Spleen.	....	76.3	77.5	75.9	....	51.0	....	64.5	....	69.6
Muscle.	75.0	74.0	75.1	74.2	44.2	74.0	45.6	42.8	49.0	72.5
						59.1				54.2
Average	....	....	....	76.1	....	66.0	66.1	....	....	66.7

Salivation, fasting and duodenal obstruction each cause 10 per cent. water loss, showing this factor to be negligible in death by obstruction.

fed series by one which lived 284 hours, so that the general average remains unchanged and it is quite safe to say that the increase of life, which in this series is nearly doubled, is due entirely to the detoxicating effect of the epithelium.

In order to show that fed jejunal and ileac epithelium exercise some special detoxicating power not yet understood but definitely recognizable, we fed a control series of dogs on the emulsified cells of liver,

TABLE 4.—FEEDING HOMOLOGOUS CELLS TO DUODENALLY OBSTRUCTED DOGS

Fed Jejunal and Ileac Epithelium			Fed Emulsified Liver, Spleen, Kidney, Pancreas and Muscle Tissue			Not Fed (Controls)		
Dog No.	Hours Lived After Obst.	Average Pulse	Dog No.	Hours Lived After Obst.	Average Pulse	Dog No.	Hours Lived After Obst.	Average Pulse
200	197	157	49	72	156	185	83	149
202	114	147	53	115	140	186	239	109
204	171	161	56	75	149	188	66	133
33	166	200	57	71	179	189	50	167
34	94	136	58	147	155	191	126	174
38	284	182	63	74	171	192	53	134
48	72	144	64	52	163	193	108	170
44	191	140	65	47	140	196	68	154
45	101	150	62	144	181	197	72	141
46	258	143	59	247	149	198	20	172
	1648	1560		1044	1574		885	1563
	164.8*	156†		104.4‡	157.4¶		88.5§	156.3

\* Average hours of life when fed epithelium.

† Average pulse when fed intestinal epithelium.

‡ Average hours of life when fed emulsion of organs.

¶ Average pulse when fed emulsion of organs.

§ Average hours of life of control.

|| Average pulse of control (at femoral).

spleen, pancreas and muscle-tissue. These animals lived a few hours longer than the not-fed controls, but it is evident that these cells had either no detoxicating action, or a very feeble one, compared with the intestinal epithelium. If we prove to have at hand some less cumbersome method than Tollens' for determining liver function, it would be interesting to use it as an index of the effect of feeding small intestine epithelium.

I have utilized jejunal and ileac epithelium clinically in two instances. First in a valuable female dog which had been imported from England about six months before, and had had "chronic stomach trouble" ever since her arrival. She, however, whelped a large litter of pups about six weeks before I saw her, without difficulty. She was a large poodle, weighing about 40 pounds. She had had complete intestinal obstruction for five days and she presented all the clinical symptoms which I have described, notable tachycardia, extreme nervousness, and great weakness in the hind extremities. On opening her, with the consent and on the advice of Dr. Blair, I removed from the oral portion of the small intestine and at a point not exactly determined, the pebble which is shown in the illustration. Her condition was very grave, the pulse running from 180 up and showing great irregularity at the apex. She was immediately put on small intestine epithelium derived from two dogs of a different breed. No one is justified in drawing any deductions from one case, but from a long experience with the symptoms of duodenally obstructed dogs, I should not under ordinary conditions have expected her to recover. The symptoms, however, gradually subsided and she lived.

The second instance in which I have used the epithelium therapeutically was in the case of a man referred to me by my colleague Jerome Lynch. The patient had had definite symptoms of obstruction for ten days, and when the abdomen was opened, an annular cancer was found which closed the terminal ileum. Not knowing whether heterologous epithelium would have any detoxicating effect, but remembering that the duodenal epithelium of frogs is capable of stimulating pancreatic secretion in the higher vertebrates, and realizing that this patient was in a desperate condition, Dr. Lynch and I decided to feed him the emulsion from a dog. Hourly doses were given until the entire epithelium from the two animals had been taken. The patient objected much more to some magnesia which we ordered, than to the dose of epithelium, which he described as "not half bad." The pulse improved and the patient lived. These cases prove nothing; they simply show that heterologous cells may be given without discomfort or harm.

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Different operative procedures were used in each. In the first, the continuity of the bowel was reestablished and most of the pent-up products of obstruction were allowed to flow to the aboral portion of the intestine. In the second, owing to the patient's condition, it was found necessary to do an ileostomy, and all the obstruction products were drained to the surface. As I have already stated, it is by no means proved that because such products are toxic to other individuals, they are necessarily toxic to their host.

#### CONCLUSIONS

The power of the liver to pair camphor and glycuronic acid is probably seriously impaired after duodenal obstruction. This can be studied by the method of Tollens, which, however, is cumbersome and may be faulty. Such decreased power of camphor-pairing is presumably an evidence of impaired liver function. This, however, is not reflected in the histologic appearance, either grossly or microscopically.

The decrease in the water-content of the tissues in duodenal obstruction is about the same as obtains after salivation by pilocarpin for four days or after fasting for seven. As this decrease produced no visible change in either case before euthanasia, it is reasonable to believe that it produces none in intestinal obstruction. The loss is 10 per cent.

The toxemia in duodenal obstruction undoubtedly arises from an interference with cellular reactions of the intestinal epithelium. The toxins undoubtedly are at least in part eliminated from the stomach and colon. If small-intestine epithelial cells of healthy animals are placed in the stomach of duodenally obstructed animals, such animals have lived nearly twice as long as not-fed control animals. This evidence is strongly opposed to the bacterial theory of origin of the toxins.

In addition to the placing of jejunal and ileac epithelium in the stomach of postoperative obstruction cases, an emulsion of them should also probably be used in colonic irrigations for the same indication and purpose.

104 East Fortieth Street.



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**DEVELOPMENTAL RECONSTRUCTION OF THE COLON  
BASED ON SURGICAL PHYSIOLOGY\***

**BY JEROME MORLEY LYNCH, M.D.**

AND

**JOHN WILLIAM DRAPER, M.D.**

OF NEW YORK

EMBRYOLOGICAL development, extra-uterine growth, and physiological requirements fuse strikingly with other factors to elaborate lesion-characters and symptoms which are not alone typical and peculiar to the colon but essentially constant, easy of demonstration and of paramount vital value. Its origin, its growth and its work, then, must be of trenchant import to all who seek a knowledge of the great gut in disease.

In the earliest period of development, the vitelline duct or yoke sac, which later may result in Meckel's diverticulum, marks the dividing line between the fore- and the hind-gut (see Fig. 1). About the third week of fetal life there appears in the posterior limb of the U-shaped tube a diverticulum which becomes the future cæcum and appendix. Thus it is clear that a portion of the small adult bowel is embryologically identical with the great gut, and this explains in a measure the apparent vicarious assumption of colon function by the terminal ileum, which will be referred to in the clinical part of this paper.

Of course it must be understood by all that it is necessary to have a thorough knowledge of the physiology as well as the embryology to make deductions. For, though the organs are allied embryologically, it does not follow that their functions are also closely associated. The proposition we have enunciated does not hold good with organs that are highly specialized, such as the kidney and heart. It applies only to organs that are less highly specialized and older in function, such as the caudad ileum and colon.

A proper understanding of the various arrests or malformations that may occur in the caudad end of the gut, often resulting in disease, may be obtained by a knowledge of its development.

About the end of the third month a rotation takes place, and the cæcum comes into position over the right kidney (see Figs. 2 and 3).

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\* Studies from the Clinic of Gastro-Intestinal and Rectal Surgery of the New York Polyclinic Medical School and Hospital and from the Laboratory of Physiological Surgery of the New York University Medical School.

In this, which has been called the second position, it rests until birth, when under *normal impulses* it gradually migrates to the right iliac fossa. In the dog, the second position is the final one, and in the light of recent studies in intestinal stasis it may very reasonably be questioned whether man would not have been much better adapted to the upright position and consequently more efficient, had the evolutionary process left his colon in the canine position. Certain it is that the operation of partial colectomy, the technic and value of which have been demonstrated by Bloodgood, and which has given such striking relief in a certain type of toxic cases, is nothing more than a reconstruction of the colon to the second or developmental position. Developmental reconstruction has been done by the authors in fourteen cases which afford basis for the clinical deductions presented. The technic of the operation can easily be followed by consulting Figs. 4 and 5.

Under *abnormal impulses* both the rotation and migration may be aberrant, with resulting malformations which are often accentuated by later growth. During the migration the appendix may be caught either posteriorly or laterally (see Fig. 6). These malformations evidently often lead to functional derangements, with consequent infection, inflammation, ulceration, pericolicitis, or new growth. In direct sequence may here be cited the clinical history of the J. family. Of seven children, four have been operated on for chronic appendicitis. Of the three remaining children, one has definite symptoms, one indefinite symptoms, one has no symptoms. A month ago the mother, aged sixty-four, who had been a chronic dyspeptic all her life, came to an emergency operation and a retroperitoneal purulent appendix was found. This is by no means an isolated instance of the occurrence of appendicular trouble in families, and Satterlee has called attention to the hereditary element in ptoses, of which appendicitis is so frequent a complication. This suggests the application to clinical study of the well-known law of heredity that, while acquired malformations are never inherited, the congenital forms are apt to be. In the type represented by the J. family, therefore, an explanation based on hereditary misdirection in the cecal migration from the second to the third position is as reasonable as is the assumption of an hereditary factor in the narrowing of the costal angle, which is an outward manifestation of ptosis, and which has been found accompanying the ptosis cases cited by Satterlee. Rovsing has called attention to the frequency with which the hereditary element is encountered.

Professor Stockard has furnished us with a specimen of intestine, from a man forty years old. The total length from stomach to anus was ninety-six inches. Nature had so beautifully maintained the balance in

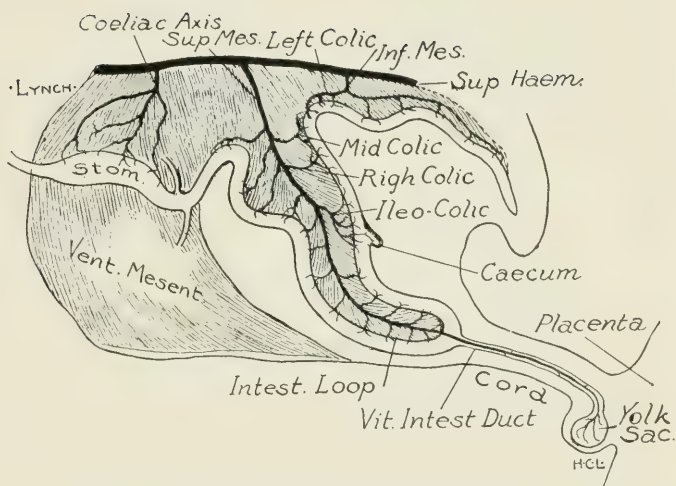


FIG. 1.—This figure shows the bud which appears on the posterior limb of the V-shaped tube, aboral to the vitelline duct. It shows not only that the transverse ileum and the colon have a common embryological origin, but that, at this period, the diameter of the small gut is greater than that of the large gut. (Keith.)

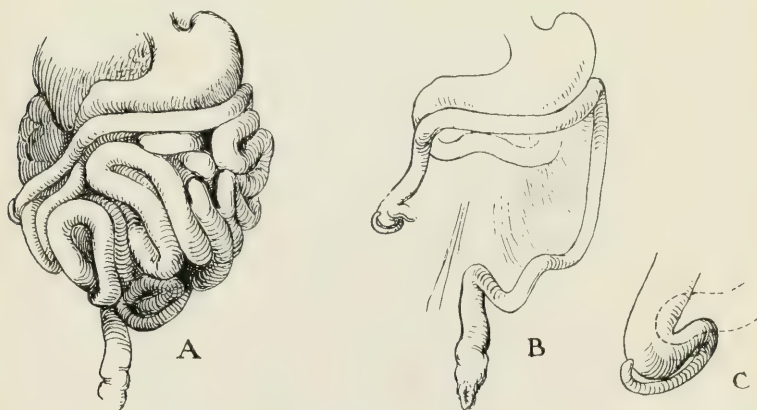


FIG. 2.—These drawings were made from a human foetus at three months. They show that the caecum occupies a position identical with that in the adult human after the operation for developmental reconstruction of the colon, namely, near the right kidney. Being drawn to scale, they also show the relative size of the large and small guts at this stage of development. (Lynch.)

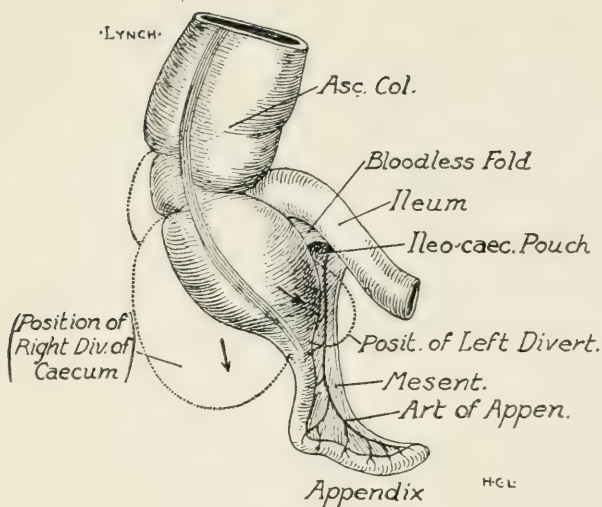


FIG. 3.—Development of the caecum, showing three primary diverticula and the primitive, funnel-shaped appendix. (Keith.)



FIG. 4.—This figure shows the extent of colon removed, and the relations to the middle colic artery. (Courtesy of D. Appleton and Company.)



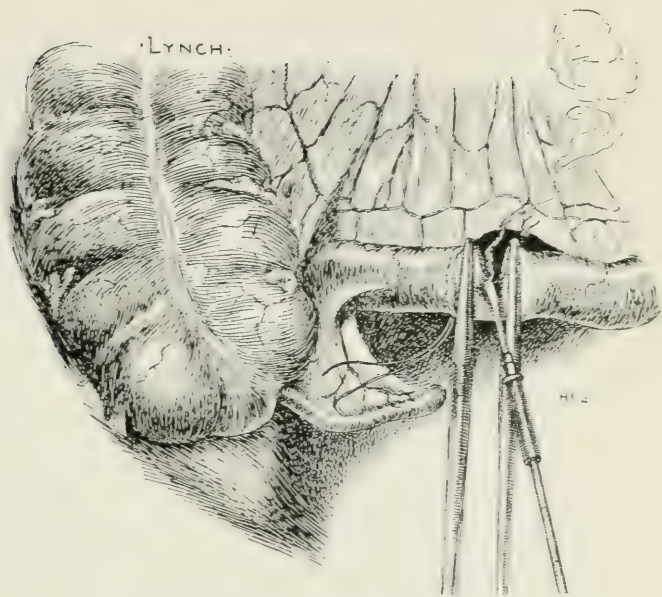


FIG. 5.—Resection of the ileum by cauterization. The same technic is used on the transverse colon. (Lynch.)



FIG. 6.—Scale drawing of a latero-externally placed appendix, which was removed from Case No. 375. Note the funnel-shaped, embryonic type of cæcum, and also the relation of this cæcum and appendix to C of Fig. 2. Appendectomy failed to relieve the symptoms. Developmental reconstruction six months later has effected a cure. (Lynch.)





## RECONSTRUCTION OF THE COLON

this case, that the circumference was found by measurement to be directly proportionate to the length.

The *function* of the colon is dual: *elimination* and *absorption*. Elimination is purposely placed first, for the reconsideration of the older physiological teaching has already come to be of great concern to surgery. Brown and Blake and Draper have shown that in dogs the doubly excluded and occluded colonic segment will fill to bursting within a few days, even if very carefully cleaned before occlusion. It is thus a pertinent question what to do with partially excluded colonic segments in human beings. Until recently this function seems to have been looked upon chiefly with academic interest. One usually and naturally associates the colon with its most evident function, that of fecal storage and discharge, overlooking its fundamentally important attributes. This attitude is not directed particularly toward the colon, but coincides with the general viewpoint regarding other matters of surgicophysiological importance as, for example, the "biliary" function of the liver and the so-called "digestive" activity of the stomach. In each the evident and supposedly important function has completely overshadowed the less evident. But the subtle cryptic functions are proving to be the very ones of greatest value to surgery and only through their interpretation can the crude applied art of to-day hope to become the finished science of to-morrow. And we are rapidly learning that only what is biologically true is of fundamental therapeutic worth. Intestinal obstruction is illustrative of this, the only therapeutic measure of any clinical value after a mechanical release of the contents from obstruction having been found through biological studies. This interesting and little understood condition is also illustrative of the importance of the eliminative function of the colon, it having been shown that, in dogs dying of obstruction, the colon was characteristically hemorrhagic, no other gross or microscopical lesion being demonstrable. This is true also of human beings. Diphtheria toxins, pilocarpine, and the metallic poisons are further examples. Indeed, an important corollary from these observations must be that colonic irrigation with or without specific biologic media may be a laudable method of treatment for the above-mentioned conditions as well as of obstruction. Indeed, the authors are inclined to believe that the well-known efficacy of continued colon irrigation is effective in large part because of the mechanical washing away of the toxins with which the water comes into direct contact. In many cases of developmental reconstruction of the colon, their patients have absorbed as much as twenty-five litres of tap water during the first post-operative week. In addition,

many litres flowed in and out, thus doubtless effecting direct elimination of toxins. This has been dwelt on by Combe. Analogies between the stomach and the colon are familiar, and one may be gleaned by studying the comparative effects of washing out the highly toxic duodenal and gastric contents, which usually accumulate in the stomach after operations on the alimentary canal, and the colon irrigations referred to. In interpreting the efficacy of stomach washing, as after morphine poisoning, we are, after all, only travelling where biology points when we assume that colonic irrigation has much the same value as gastric lavage. Further analogies between the stomach and the colon will be alluded to later on.

The eliminative diarrhoeas of constipation, of the syndrome called goitre, of nephritis, of syphilis, after the giving of salvarsan, further demonstrate that surgically the colon should be looked upon first as an excretory organ. But animal experiments show clearly that this applies only to the caudad colon. If this be true in the human, as seems reasonable from analogy and observation, then we certainly should hesitate to deprive any individual of so very important a function by the operation of total colectomy, and this irrespective of further metabolic considerations. Surgery, ceasing to be merely an adjunct to medicine, is rightly becoming the active collaborator of chemistry and physiology.

In studying the absorptive function of the colon, surgery has come further to the aid of physiology. Certain new facts of undoubted importance in human therapy have been learned by making use of surgical material, which recent operative procedures have afforded. Any digestive and absorptive function of the colon may naturally be taken on by its embryological prototype, the caudad ileum. Our surgical cases seem to prove this, and these human studies corroborate Cannon's animal findings as to the close physiological relationships between stomach and cæcum.

From a digestive stand-point the stomach and cæcum are unimportant. They are both receptacles, and if their motility is not impaired, they normally retain faint traces of digestive functions. The loss of these latter are not felt by any individual if the former is retained. Thus, every observer knows that the objective symptom called *achylia gastrica* may exist without any subjective symptom developing, provided that gastric motility remains normal. Von Noorden (*Path. of Metabolism*, p. 186) says, "Protein putrefaction in the stomach reaches a high degree only in the most exceptional cases, and only when both the *secretory and motor functions are completely out of order.*" Theoreti-

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cally, as just stated, any digestive and absorptive function of the colon should naturally be taken on by its embryological prototype, the caudad ileum. Clinical experience and animal experimentation prove to the authors the stability of this hypothesis, based, as it is, on embryology. Their studies after ileostomy support it.

It is well at this point briefly to review the absorptive and related functions of the colon, as given by physiologists, and then to consider the further details of our researches.

In a recent paper Hertz says, "Antiperistalsis does not occur in man under normal conditions: the ileocecal sphincter does not always prevent regurgitation into the ileum. . . . There can be no doubt that the function of the sphincter is, as Keith originally suggested, to prevent the *contents of the ileum passing too rapidly into the cæcum.*"

This function is supplemented by the normal inhibition that is resident in the terminal ileum and can be accentuated under physiological requirements. The preservation, in part or in whole, of this inhibitory segment will, in the future, undoubtedly be an important factor in determining the point at which the ileum is to be cut, prior to ileocolostomy. This is supported by our clinical findings.

Drummond says, "After ileocolostomy the dilated coils of small gut adjacent to the colon *assume somewhat the functions of the large gut.*"

Von Noorden states, "Numerous experiments introducing protein bodies (myosinogen, egg albumen, and casein) into the rectum have shown conclusively that an absorption of natural protein *takes place in the rectum and colon.*"

Chittenden says, "In the large intestine . . . the last portions of available nutriment are absorbed."

Howell states that when the contents of the small intestine pass the valve they contain a certain amount of unabsorbed food material. "The food," he says, "in this portion of the canal is more or less liquid, and its presence sets up running waves of constriction which, beginning somewhere in the colon, pass toward the ileocæcal valve. These waves occur in groups, separated by periods of rest. The pressure of the ileocæcal valve prevents the material from being forced back into the small intestine. The value of this peculiar reversal of the normal movements of the bowel at this particular point would seem to lie in the fact that it delays the passage of the material toward the rectum, and, by thoroughly mixing it, gives increased opportunities for the completion of the process of digestion and absorption." This



colonic digestion, it is conceded, must take place through the action of the enzymes, which are brought down from the small bowel and which, under favorable conditions, continue their activity in the colon. In this way it is estimated that at least from one to seven per cent. of the undigested foodstuffs, chiefly fats, are utilized. Now, if this is so, it means that a patient whose colon is static may lose this amount of food. Sir William Macewen was so impressed by this and by a case that came under his observation that he made the statement that, if the chyme was allowed to escape cephalad to the ileocæcal valve, the patient would lose weight, and that under those circumstances artificial feeding should supplement the ordinary diet. Our experience is at variance with this. Not alone is the loss of the normal absorptive function of the colon insignificant, but it is greatly overbalanced by the damage done to the organism through the toxic action of the end products of bacterial proteid dissociation which frequently occurs in the ill-developed, slowly emptying cæcum and ascending colon. One characteristic result of this toxæmia is mental depression, which may even go so far as to result in mania.

CASE No. 1832 while at school attempted suicide three times; was treated by competent men from a neurological stand-point, and was finally operated on by Tuttle, with complete symptomatic relief.

CASE No. 2061 had been imbecile and bed-ridden for a year but recovered after ileostomy. Her debility was so great that the operation had to be done under local anæsthesia.

CASE No. 1180 (Path. No. 2081) presents the following data: Ileostomy, male, aged thirty, physician, weight 120 pounds, operated on April, 1912, for relief of acute inflammatory condition of colon with multiple polyposis. Owing to the existence of a common mesentery for ileum and cæcum, both were brought outside the wound. Both were opened on the ninth day. Soon thereafter the following observations were made. The reaction of the ileac contents was always acid. The flow of contents was not constant, often being interrupted for several hours. Its consistency varied with the diet; excessive nitrogen caused fluidity; on mixed diet content was fairly well formed; sometimes very hard, when large, stick-like movements would be passed. No putrefactive germs, either anaërobic or aërobic, were found. No fecal odor was ever noted. Occasionally the odor was pungent and distinctly unusual. The only enzymes ever present were amyl-opsin, a marked, steapsin, a faint trace. Gain in weight over twenty pounds.



Another function that physiologists attribute to the cæcum and ascending colon is the absorption of water; all the water normally shall have been absorbed when the contents reach the mid-transverse colon. Surgeons have made ample use of these observations in support of various technical procedures, and a careful study of post-operative conditions shows, in some cases at least, that their premises or conclusions, or both, were incorrect. Our studies in the surgical physiology of the parts strongly suggest that embryology and physiology should always precede pathology as a basis for surgical therapy. Indeed, Bloodgood, doubtless the best qualified surgical pathologist living, states that the future hope of surgery lies in physiological chemistry.

Obviously, one cannot properly reason from a secondary basis alone, such as is offered by pathology, without having constantly in view also the elemental or primary sciences of embryology, physiology, and chemistry. Without, therefore, a knowledge of the intimate co-relationships that exist between all parts of the body in general and certain parts in particular, applied, or, as it is frequently and erroneously called, "practical" surgery cannot be further developed. Structures of common embryological origin, like the cæcum and caudad ileum, may show the greatest possible morphological variation, and yet lend themselves favorably to applied reconstructive surgery when this is done in harmony with both their origin and their function. Thus, the predominant conception to-day that the caudad colon, that is, the part aboral to the mid-transverse line, is capable of vicariously assuming the functions of the cæcum and ascending colon, as after ileocolostomy, may be correct, but is, in our opinion, incomplete. Surgeons have been led astray by the gross morphological differences between the caudad ileum and the cæcum, forgetful of the facultative co-partnership that must just as truly exist between these embryological units as between the morphologically identical portions of the colon. This, at least, seems to us a reasonable basis for explaining the observed interchange of function between the ileum and the colon, which we have herewith recorded. It may also serve to explain the present difficulty in forecasting the end-results after such operations as ileocolostomy. After the implantation of the ileum into different parts of the colon, a persistent diarrhœa or constipation has been known to occur. As a general rule, the diarrhœa ceases after a short time, but the constipation has proven to be a much more difficult problem to deal with. The explanation of these two facts is now apparent: the vicarious assumption of colonic function by the ileum is almost sure to come; it absorbs water and forms the fæces; but the constipation, a pathological condition which existed in the ileum

previous to operation, obviously could not be influenced by the mere change of ileac position brought about by this type of operation. It might be influenced, perhaps, as shown in author's case No. 2012, by the exclusion of the inhibitory segment of the terminal ileum. Here the anastomosis, owing to adhesions, was made considerably oral to the termination of the foregut and, consequently, oral to the inhibitory segment. Indeed, this operation must increase the normal inhibition belonging to the part, thus aggravating the symptom. This increase of constipation has been noted in practice. This is quite distinct from the constipation due to anastalsis, and which frequently packs the cæcum after ileocolostomy, until its entire removal is necessitated. Lane states that this may be necessary, and Patterson places the instance at 5 per cent. or over. Probably it is much higher. Careful clinical study along these physiological lines is obviously indicated, so that surgeons may re-adjust their technical procedures upon a sounder basis. The ileac constipation is as yet open only to medical therapy and for this reason every effort at differential diagnosis between the two should be made.

Hertz presents some facts of interest here. He says, "An accumulation of chyme occurs in the last few inches of the ileum, where it remains and undergoes digestion, actually for a greater period than in the stomach. The normal ileac stasis is increased in all conditions leading to spasm or to the inhibition of the normal relaxation of the ileocæcal sphincter."

Conclusions based on the X-ray alone may lead one into grave error, owing, first, to the fact that röntgenologists are still unable to differentiate between stases due to mechanical and reflex causes, as, for example, between a mechanical kink and an ileac constipation, and, second, to the fact that it has not yet been definitely settled whether bismuth traverses the gut at the same rate as ordinary food, or slower.

What are our further proofs that cæcal digestion is negligible?

At a certain period of fetal life, as already said, there is little difference between the morphological appearance of the small and great gut. The latter, at first much smaller than the former, contains villi which are later obliterated, the process of obliteration not yet being definitely settled. It is assumed that Lieberkuhn's follicles are inverted villi. If so, they may, under the pressure of physiological requirement, revert to the fetal condition and vicariously functionate as villi in fat absorption. But fats must be emulsified before they are fit for absorption, and under the catabolic influence of lipase, which is present

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in the colon as in all other tissues, emulsified fats may here be digested. In support of this, Tuttle claims to have increased the weight of a patient by the injection into the cæcum through a cæcostomy of emulsified fats. For the purpose of surgical physiology, however, it appears that the amount of fat absorption in the cæcum and ascending colon is of academic interest only.

Carbohydrate and proteid absorption in these parts occurred in Case 180, Path. N. 2081, as follows: Grammes, 30 dry peptonoids were mixed with grammes 113.4 warm water and introduced into the rectum at 11 P.M. At 8.30 the next A.M. the bowel was washed out from above with sterile water and the residue examined. Analysis of the peptonoids introduced was as follows (Lab. of Physiology, Cornell University): Protein 39.81, carbohydrates 50.05, water 4.72, ash 5.32.

Analysis of washings showed that one-half the sugar and nitrogen had disappeared. There was considerable fermentation which probably had a good deal to do with the disappearance of the sugar.

The nitrogen was in the form of amino-acids. This experiment suggests that proteins in the form of amino-acids may be absorbed from the colon. Normally, however, the amino-acids are absorbed in the small gut only. Under abnormal conditions of incomplete hydrolysis, peptones and other provisional products of protein digestion probably enter the cæcum, there to be converted by the proteolytic bacteria into the highly toxic by-products which, directly or indirectly, cause the familiar symptoms of stasis. Combe has called attention to the necessity of removing them by enemata. Adami regards the condition as a subinfection. Abderhalden has proved that the final product of physiological protein digestion is the amino-acids, having recovered them from the blood. It is clear, therefore, that for the purposes of modern surgery protein digestion in the colon is as unimportant as it is in the stomach.

Rectal alimentation has long been a comforting and satisfying therapeutic procedure in the hands of the profession. It was ancient medical history when Hippocrates was a boy. Recent physiological studies, however, show that the hypnotic influence of this old method of vicarious feeding has been at least as great upon the physician as upon the patient and his awe-struck family. Probably, the good which it is conceded may follow it has been due to the therapeutic action of the water and in no way to the food.

Our medical heritage is almost as rich in bewildering stimuli as our atavistic, which long antedates the batrachians. The one moulds our therapeutic ideas; the other fashions our form. We are encum-



bered with a faith based upon a horde of inherited misconceptions, and the subject of rectal alimentation is only one of the many instances which prove it. Far be it from the province of surgery to set these right; surgeons are not Hamlets, but it is fair to say that the recent rapid progress of colonic therapy has contributed more than any other single factor of the day to endorse reconstructive ideas as well as applied procedures, and to show the pressing need of coöperation between the laboratories of the fundamental sciences and the hospital operating rooms. The unfriendly attitude existing in the past between physician and surgeon was a misunderstanding arising, as always, from ignorance and is rapidly being put aside. Medicine has evidently been at fault in treating, as in dyspepsia, the peripheral manifestations of some remote insult to the sympathetic system. Surgery, equally undeveloped, was at first simply the emergency tool of medicine, necessarily poor and crude. Gradually light has come from physiology, embryology and chemistry, until to-day surgery is able to offer, in selected cases, a therapy which, in removing the cause of disease, often effects a true cure. Such therapy is based on the incontrovertible premise that human beings are normally healthy animals and that for many chronic diseases there is a mechanical cause.

Intestinal stasis with its long train of protean and distressing symptoms is evidently a common ground upon which physician and surgeon may profitably meet to discuss, without bias or prejudice, the therapy of the future. Whether the developmental reconstruction of the colon herewith described will prove to be of lasting value may, perhaps, be doubted, but one argument favoring its continuance may well be its basis on embryological truths. It aims to correct a congenital deformity and is thus a form of orthopædic surgery. This speaks for its continuance, for the repair of congenital deformities must obviously continue long after the surgery of tumors and inflammations has happily passed away.

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**CONTRIBUTION TO THE SURGICAL PHYSIOLOGY OF  
THE COLON\***

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THERE are three modes of approaching the study of functional abnormalities in the human colon. The first is based upon the influence of heredity and environment, and may therefore be looked upon as biologic in character. The second is based upon facts gleaned through experiments upon the lower vertebrates, through the help of which a good deal may be learned regarding the surgical physiology of the part, and these studies may properly be supplemented by biochemical observations upon human beings in whom the path of the ingesta has been shortened, as, for example, by ileostomy. The third source of information is to be had by a critical clinical interpretation of the subjective and objective changes in human beings observed before and after therapeusis.

It seems clear to the essayists that our knowledge of the colon at this early day is not far enough advanced to justify any exclusive claim for the furtherance of this or that special form of therapy, be it so-called medical or so-called surgical. They therefore present herewith certain data, gleaned as outlined above, in the hope that it may be of use to others as a basis for inductive study, and in the conviction that time and a wider acceptance of the fundamental sciences will soon bridge the rapidly narrowing channel which unfortunately still separates the therapeusis of the physician from that of the surgeon.

Man alone among the mammals possesses the highest intelligence and the most unstable digestion. There are two important phylogenetic reasons for this, and these are often supplemented by errors in ontogenetic development. Until birth he is the variable product of two forces: those hereditary tendencies resident in the germinal material itself, lasting throughout his life, and those imposed upon him by

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\* Read before the American Society of Gastro-enterology, Baltimore, 1915.

the peculiar conditions of his environment during the period of gestation and continuing more or less until death.

Phylogeny ordains that man shall often bear a heavy, segmented colon, semi-herbivorous in type, and that he shall walk upright. The herbivorous colon is obviously designed to be supported by the anterior parietes; man's habits of life deny this support and subject the badly and imperfectly suspended organ to the pull of gravity for at least half of his life. Shaler<sup>1</sup> considers that the upright position has been paramount among all other factors in fixing the length of the life of man.

Ontogeny furnishes many opportunities for faulty growth and position. On account of the very complex human development, during which the individual foetus must follow a narrow and devious path of extreme antiquity, there are innumerable opportunities for arrested or irregular form.

Man, in other words, while following his long and complex course of development, is swayed by two differing forces, heredity and environment. An appreciation, therefore, that even in his alimentary canal he is the product of these complex forces must be helpful in understanding the maze of adult variations of form, position, and function, which confront the student of gastro-enterology. Our course of reasoning must be changed from the deductive to the inductive form of thought. Deficiencies in type must be recognized by the diagnostician early in life if therapy is to hope to make amends for nature's shortcomings in any given individual. In the purest type you can collect, there are hundreds of species.

Wiedersheim has collected one hundred and eighty variants of the hereditary type in human beings. The persistence of the lanugo as seen in the Russian dog men, or of the palmar muscle which enables babies to support themselves from a rod and grown men to bend small coins, and which normally disappears, are excellent examples of the tenacity of early characteristics. How logical it is, therefore, to trace many of the colonic variations which we know invite disease to the persistence of embryonic conditions which may be much less remote in the evolutionary scale, and, because of modern facilities such as the X-ray, just as easily demonstrated. The old-fashioned notion as to inheritance of heart and kidney disease, discredited on the ground of non-transmissibility of acquired conditions, may really be due consideration if it be true, for example, that colonic toxæmia is a factor in the causation of sclerosis. Evidently, in these days of preventive

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<sup>1</sup> Shaler: Individual.

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medicine when the pressure in the social fabric is so acute, and when, just because of our rapid evolution, a very highly developed individual may mate with one of lowly heredity, it must become an engrossing task to find therapeutic methods wherewith to meet and offset the products of disregard of the laws of eugenics. Many a poor, ill-conditioned, clammy-handed child, backward in its studies, seemingly lazy, inefficient, and ill-tempered, is, in light of recent knowledge, not intrinsically delinquent or even intellectually deficient, but often the unhappy result of a congenital dysmorphia of the stomach or cæco-colon. Such defects may be, as stated, due to the inheritance of characteristics unsuited to the human type.

Comparative anatomy<sup>2</sup> of the vertebrates supports the hypothesis of developmental relationship between cæcum and stomach. For example, in the horse, the cæcum and cæcal colon are well developed and complex, the stomach being simple; on the other hand, in ruminants, as the cow, the stomach is complex while the cæcum is simple.

In carnivora the cæcum is naturally small and rudimentary, while in man, who leans to the side of the carnivora, the cæcum probably is of little use and is normally small. Nature has made no provision for an over- or ill-developed cæcum in man, the stomach having taken its place. However, the cæcum not infrequently takes on the herbivorous type. This has all the disadvantages and lacks the delicately adjusted mechanism and advantages of the true herbivorous form. Clearly then this cæcum, from the stand-point of development and usefulness, becomes not alone useless to the human economy, but actually detrimental to it. Such a condition is not to be wondered at when one considers that very divergent developmental paths have been taken by the individual and by its aberrant organ. Bryant<sup>3</sup> has put the classification of human beings into herbivorous and carnivorous upon a firm basis. Furthermore, normally limited in circulation, when the cæcum is over-developed, the blood supply is extremely deficient and weak. As its motility is impaired and its morphology perverted, its current slows and it begins to harbor and to disseminate the unidentified but definitely proven toxic substances which result, indirectly, in disease.

The weak point in the small gut is the duodenum, for its support is deficient. Dilatation often occurs here and may be in turn transmitted to the stomach. Barber's<sup>4</sup> studies show the relation of the

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<sup>2</sup>Keith: Human Embryology and Morphology.

<sup>3</sup>Bryant: The Carnivorous and Herbivorous Types in Man, Boston Med. and Surg. Jour., March 4, 1915.

<sup>4</sup>Barber: Dilatation of Duodenum, ANNALS OF SURGERY, 1915.



autonomic system to dilatation and are not in direct accord with the views of those who consider the mechanical factor of support, or traction upon the mesentery as paramount. He has demonstrated by a series of animal experiments the different effects upon any tube in the body of partial or complete obstruction. Briefly, partial obstruction of the ileum results in duodenal dilatation, whereas complete obstruction is followed by duodenal contraction and ileac dilatation at the point of obstruction. He has also shown that a close correlation exists between the ileocæcal and the uretero-vesicle valves as regards their importance to the economy. His conclusions, shortly to appear in the *ANNALS OF SURGERY*, are as follows:

"The whole muscular arrangement appears quite analogous to that described for the ureter by Bardeleben, and undoubtedly furnishes adequate anatomical explanations for the analogous physiological mechanism for the small intestine and the ureter.

"It is extremely difficult and hazardous to correlate all this experimental and anatomical material. It is evident, however, that an incomplete obstruction permits the free intercommunication of the duodenal and cæcal centres through Auerbach's plexus, whereas, a complete obstruction interferes with such relationship. Furthermore, abnormal cæcal stimuli, whether from an inflamed appendix or an incompletely obstructed cæcum, may have the same cumulative effect upon a duodenal centre as does the obliteration of all such stimuli together. In other words, we should expect in the first case (incomplete ileac obstruction) a duodenum laboring to the point of fatigue and dilatation under a plus physiologic load, and in the latter case (complete ileac obstruction, incomplete cæcal obstruction, and typhilitis) the conservation of duodenal contractile power and a more tonic duodenum."

Turning to the development of the individual colon we find certain critical periods which may be classified as follows: The first coincides with the appearance of the buds from the vitelline duct, from which are developed the hind- and fore-gut. The second is at about the third month when, normally, the bowel rotates. The third is the period of adhesion or fusion, after birth.

*The stomach and cæcum have but two important functions, those of storage and motility. All others are negligible.* Because of normal man's leaning toward the carnivorous type and diet, and because of his upright position and numerous environmental factors, the cæco-colon, so to speak, has outlived its usefulness, being but a vestigial remnant of the organ so essential to the herbivora. We do not find that this is true of the remainder of the great gut.



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Any other function possessed by the ascending colon and cæcum can be cared for by the caudad ileum. This is reasonably to be explained upon a biologic basis, for although differing widely in form, they have a common embryological origin.

In general, then, we may assume that the acquisition of certain intestinal malformations is evidence of hereditary predisposition. Some ill placed individuals, as we shall show later, yield to it, others do not. A plausible hypothesis as to the frequent occurrence of an ill adapted pseudo-herbivorous cæco-colon in man is perhaps that his remote ancestors were very imperfect in type and that these have perished. Mutations may arise *de novo*, and we are ignorant regarding their source. Man was unquestionably dark originally, the albino being a mutation.

All digestion takes place between the pylorus and the caudad ileum. Even the absorption of water, we have shown in our human experiments by ileostomy, not to be obligate as regards the colon. The reaction is acid in the ileum and alkaline in the cæcum. Human beings, after ileostomy, gain weight and pass solid fæces and odorless gas.

The basis for the foregoing is as follows: Case 180 (Lyon). Ileostomy for multiple polyposis, April, 1912. Six months after operation stool examinations showed nothing unusual except carbohydrate fermentation and a decidedly Gram-negative bacterial flora. The only enzymes found were amylopsin, decided, and steapsin, a faint trace. This has been confirmed by MacFaydyen, Nencki, and Sieber.<sup>5</sup> The reaction was tested daily for over a year and was found to be always acid. This is also supported by the authors above cited. They state, "Of noteworthy significance was the acid reaction throughout the whole length of the small intestine due to organic acids, chiefly acetic acid. The milk acids are neutralized by the alkaline producing mucosa. The neutralization of the HCl of the stomach takes place in the upper portion of the duodenum." Authors never found HCl. "All analyses showed that secretion of the small intestine contains natroncarbonate, and it was interesting to see in this patient how the mucous membrane of the ileum was alkaline in reaction but the contents acid. Alkaline reaction of the mucous membrane of the colon was much more intensive than that of the ileum. The alkaline reaction of the chyme begins in the large intestine." The importance of these observations, which are in accord with our own as regards bacterial growth in the ileum, cannot be overestimated.

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<sup>5</sup> MacFaydyen, Nencki, Sieber: *Archive für Exp. Path. and Pharm.*, 1891, vol. 28.

Ileostomy affords opportunity for critical study of the accuracy of X-ray findings as regards motility. There appears to be a difference in the time taken by bismuth and by ordinary food-stuffs to reach the cæcum. It is reasonable to expect a difference, bismuth being a substance foreign to the gut. Of the one hundred and sixty-four feeding experiments checked by carmine and charcoal made by Dr. Lyon, upon himself, the average time of first appearance at the stoma was 4 hours 57 minutes, the maximum being 6 hours, the minimum 4 hours 15 minutes. Addition of agar-agar gave 3 hours 45 minutes. Average time total emptying 11 hours 56 minutes; maximum 14 hours 30 minutes; minimum 8 hours 30 minutes. Consistency varied with food as follows: Meat diet yielded liquid stools; carbohydrate solid.

The following quotation from Dr. Lyon's observations upon himself are valuable. Shortly after operation and evidently before establishment of the vicarious compensation already referred to, he says, "Intense thirst generally during evening. After drinking eight or ten glasses am satisfied. At such times noted no change in the movements. Chicken and turkey leave more undigested muscle fibres than any other foods. Riding on trains always delays motility. Bananas of great value when bowel is sluggish."

One of the most interesting physiological observations to be made after an ileostomy has bearing upon referred pain. If the finger is passed into the ileac stoma or through the valve, pain occurs at the umbilicus and frequently over the splenic flexure. Nausea always and vomiting sometimes results.

Accidentally a concentrated stock solution of sodium chloride was poured into the colostomy of a physician. Severe pain in pit of stomach, shock, and collapse resulted. Intense thirst for 24 hours was followed by gradual recovery. After ileostomy, patients are able to detect immediately the entrance of even the smallest particle of ileac contents into the resting colon. Dr. Lyon found that dizziness, faintness, and cold sweats were the invariable subjective symptoms of this accident. The same symptoms but in less degree were brought on by inserting the finger into the colon. Every patient upon whom we have done ileostomy has experienced the same symptoms. Is it unreasonable to assume that certain of the familiar symptoms of so-called colonic toxæmia may be due to analogous mechanical conditions, whatsoever these may be?

In conclusion, we believe that the influence of heredity and environment upon the functional abnormalities of the human colon is paramount and that these fundamental biological factors are due further consideration. Attributing pathological conditions of the colon to any

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single factor is a grave error, as isolated deficiencies may be compensated for. In the lower vertebrates, surgical physiology of the valvular mechanisms of the body proves that many complicated factors go to maintain the balance. The valve is the first line of defence; the physiological integrity of the tube is the second. Symptoms will not necessarily follow impairment of one; a valve is useful but not essential. In man, laboratory studies show that no matter how severe the derangement within the bowel, so long as compensation is maintained the body is protected; let the defensive power be weakened, however, and symptoms immediately arise. An excellent example of this has been noted by Bloodgood in his differing results following colonic resection for malignancy and benignancy.

Symptoms, therefore, are often misleading and in themselves are an inadequate basis upon which to form opinions for diagnosis. They must be carefully correlated with the facts of the fundamental sciences and their absence does not necessarily mean normal function.

**CASE HISTORY.**—*Pre-operative Data.*—Typhoid 17 years ago. One year later diarrhoea, 7 to 8 liquid stools a day. No blood. Winter intermission. This occurred for 3 summers. Total intermission for 5 years. Winter intermission until 1911. Then alternate diarrhoea and constipation. Noticed blood for the first time. Ten to 20 stools a day. Severe colicky pain relieved by stool. Localized at splenic flexure and left ileac region. Obligated to give up work owing to extreme nervousness and loss of mental coördination. Great physical prostration—in bed for weeks at a time.

*Operation.*—Complete ileostomy.

*Post-operative Data.*—1. Cessation of pain except at irrigation. This gradually disappeared.

2. Subjective symptoms: *Attacks of faintness*, clammy sweat, cold extremities, weakness and great prostration. Pulse rapid and at times irregular. In 8 minutes desire to defecate followed by small muco-sanguinous discharge with some relief of symptoms. Average duration of attacks 3 hours. Frequency of attacks: Varying from 1 to 3 a week, depending upon the amount of work done. These diminished in frequency and ceased after 6 months. Introduction of foreign body at stoma into resting colon caused same symptoms.

3. Thirst: Intense thirst for first 2 months gradually disappeared as movements became solid. Shows vicarious assumption of colonic function by ileum.

4. Urine: Until solidity of stool, urine markedly diminished. After solidification about 800 c.c. Nitrogen partition made one



year apart at Cornell and Yale Laboratories showed normal metabolism.

5. Sense of fecal discharge: Absent until solidification of contents, and more marked after contraction of stoma. Never painful.

6. Character of stools: Formed stools and often segmented showing layers of food stuffs.

7. Reflex: Occasional cardiospasm with burning sensation in stomach. Occurs once or twice a month without apparent cause, lasting for 2 or 3 days; disappears spontaneously.

8. Rectal discharge: First 6 months irrigations every 12 hours. Some bloody mucus without pain, always from the rectum, passed between these intervals. Second 6 months, irrigations every 24 hours. No discharge except when voiding irrigation. Second year, daily irrigations, practical cessation of blood, and diminution of mucus. End of third year, comfort with bi-weekly irrigations. Discharge reduced to small amount of mucus with very occasional small blood clot.

9. Work capacity: Mental, carrying on regular professional duties. Restoration of normal mental coördination. Complete physical restoration. Able to walk ten miles or row a boat all day.

10. Food: Intense hunger first year after operation, three heavy meals a day. Second and third year normal appetite, food requirement about one-half what it was the first year.

11. Effect of ordinary foods: Nothing ordinarily interferes with solidity of stool.

12. Effect of tainted food: Ileostomy prevents the pain of so-called ptomaine poisoning, the first symptom being continual liquid stool.

13. *Dressing*.—Once a day on arising at time of irrigation. No further attention until 3 P.M. Bag then emptied, it contains the breakfast. Usually again at 8 P.M. This contains lunch. And again upon retiring, this contains part of dinner. Dressing consists of zinc oxide ointment and powdered starch. Night dressing: Cover abdomen with zinc oxide and powdered starch, make a quadrangular space with three-inch cotton roll, stoma at centre. Cover with a layer of cotton, hold in place with a roller bandage over which place a many tailed bandage.

14. Mechanical device: A Delatour apparatus modified to prevent obstruction due to kinking of bag when sitting upright.

15. Gain in weight: First year 17 pounds; second year 6 pounds; third year stationary; total gain 23 pounds.

16. Conclusions: After solidification of the faeces, which occurs in six weeks, there is so little discomfort from an ileostomy as compared to relief from cessation of symptoms, that we unhesitatingly advise its employment.

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*Additional Data.*—Stool: 1. Odor: A slight sour odor never offensive; no fecal odor.

2. Reaction: External surface of fæces alkaline; centre acid.

3. Color: Varied with diet. Meat, dark brown. Potato, dark brown. Baked beans, apples, turnips, light brown. Spinach, string beans, green. Crackers, oatmeal, bread, milk, light yellow. Eggs, black.

4. Form of stool: At first liquid; in six weeks some formed stools. At the end of third year all formed except upon liquid diet.

5. Segmentation: At the end of three years the stools showed little segmentation.

6. Marking of stool: A capsule of carmine, .3 grammes or charcoal given just previous to the meal. Or certain foods, as peas or corn, whose cellulose envelope remained undigested.

7. Time of appearance of foods: In 164 observations on a mixed diet the average time of first appearance was four hours and fifty-two minutes. Shortest time three hours and forty-five minutes. Longest time six hours.

8. Time of complete passage: In 164 observations was eight hours, thirty minutes was the shortest time, and fourteen hours the longest, the average being about ten hours and thirty minutes.

Diet	First appearance	Last appearance
Turkey, potato, turnip, bread.....	4 hrs. 30 min.	9 hrs. 30 min.
Steak, mashed potato, bread .....	5 hrs.	11 hrs.
Scrambled eggs, toast, coffee .....	5 hrs. 15 min.	11 hrs.
Roast veal, potato, bread, lima beans . . .	4 hrs. 50 min.	12 hrs.
Roast lamb, potato, bread, boiled rice . . .	4 hrs. 15 min.	9 hrs. 30 min.
Sausage, wheat cakes, coffee .....	4 hrs. 40 min.	12 hrs.

9. Time of movements: No regular time, but began from four and one-half to six hours after ingestion and continued until all had passed.

10. Test for enzymes: Amylose, very marked reaction; steapsin, faint reaction; trypsin, negative.

Solidity of stool: From 11 to 13 per cent. solids on mixed diet.

12. Absorption from colon: Thirty grammes of dry peptonoids in two ounces of water injected into rectum in knee-chest position at 11 P.M. Washed out with sterile water at 8 A.M., examination showed one-half of the sugar and nitrogen had disappeared. There was marked fermentation and therefore probably little absorption. Analysis of dry peptonoids:

Protein (N. 6.25) (probably amino acids).....	39.81
Carbohydrates (mostly lactose) .....	50.05
Water .....	4.72
Ash .....	5.32
Fats—extremely small.	



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13. Effects of bismuth: Patient given a meal and time of appearance noted. The next day the same meal preceded by one-half ounce of oxychloride of bismuth. Time of first appearance showed delay of one-half hour. When one ounce was taken the delay was five hours.

Experimental meal .....appeared in 4 hrs. 45 min.

Experimental meal plus one-half ounce bismuth.appeared in 5 hrs. 15 min.

Experimental meal plus one ounce bismuth....appeared in 9 hrs. 45 min.

Lemonade: A glass of lemonade caused an increased flow of bile as shown by abundant dark green liquid at stoma.

Cathartics: One-half ounce of Epsom salts caused a liquid stool at stoma in about two hours.





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## THE INFECTED COLON AND ITS SURGERY.\*†

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AND

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NEW YORK.

*(Introductory Note.*—This paper is not a plea for either so-called surgical or medical therapeutics, but a simple chronicle of certain facts which the authors have obtained through experimentation on animals, through laboratory studies on human material, and from clinical results.)

Bouchard, after Claude Bernard, gave added impetus to the study of autointoxication. Roger, Metchnikoff, and Combe, working along somewhat divergent lines, have made our knowledge of this interesting symptom-complex more complete. Adami, after reviewing this earlier work in collaboration with his own extensive studies, concluded that the process should be properly considered a subinfection of bacterial origin. Combe believed that the origin of the toxemia was to be found in the bacterial hydrolysis of the proteins. Metchnikoff was also inclined to this view and most of the present day therapeutics is based upon this con-

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† Studies from the Surgical Clinic of Colonic and Rectal Diseases, New York Polyclinic School and Hospital and from the Laboratory of Surgical Research, New York University.

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ception. His idea is that the protolytic anerobic bacteria are the toxic agents—these thrive best in the alkaline secretion of the cecum and cecocolon. That the reaction of the ileum is acid is taken to explain the fact that these bacteria are seldom found there save under pathological conditions. Under this hypothesis originated the sour milk, lactic, and succinic acid treatments.

From a surgical standpoint it is necessary to include not alone the lesions caused by substances formed through the vital processes of the organism, which is Combe's conception, but also those arising from destructive infection of the bowel wall, which in a sense is not true autointoxication, but which is essentially a surgical disease. Surgeons can at present do no better than find a means to prevent the absorption of the toxins from a given part of the bowel, however these poisons may have been created. Thus, we limit ourselves here to a consideration of partial obstructions by whatsoever cause, and of colonic infections which are destructive or inhibitory of the normal functions of this part, particularly those functions which protect the body from infection. This amounts to nothing more than a conservative extension of surgical therapeutics to the colon. Does it not seem logical to apply the same surgical principles to the colon as to other organs? Most acute and chronic purulent colonic infections are surgical from the start, and the future functional efficiency of the organ and of the individual depends upon early recognition and proper treatment.

The colon is pouched at either end, and its entrance and exit are guarded by valves. It is widest at the cecum and narrowest at the rectum. Four angulations give to this organ potent pathological possibilities. Three gross features distinguish it



from the small gut: (1) The teniæ, (2) the appendices, (3) the haustra. Not being a highly specialized organ, the colon is subject by the laws of heredity to great variations both of size and of position—specialization results in a rigid adherence to a fixed form. The greatest variations are seen, as would be expected, in the cecum and sigmoid. Microscopically, except at the apex of the cecum, the most important surgical consideration is the relative scarcity of lymphatics and the absence of villi. This suggests what has lately been proven: that the digestive function of this organ is nil. Auerbach's plexus has recently come to be of great surgical importance because of our increasing surgical interpretation of the function of the autonomic system. The terminal ileum, the appendix, the cecum, and colon have a common origin. This has an important bearing upon surgical physiology. Obviously, the entire alimentary canal, particularly its caudal portion, is ill-adapted to the gravity strain incident to the upright position, even when the support and the torsal development have been most favorable.\* A consideration, therefore, of the biological forces constantly at work is of great interest to the diagnostician and to the operating surgeon. Hereditary tendencies resident in the germinal material itself, lasting throughout life, and those imposed by the peculiar conditions of man's environment, combine to yield a high percentage of ill-adapted cecocolons. Bryant has shown that an herbivorous and a carnivorous classification of human disease is possible, and it is evident that in no part of the body is this more true than in the cecocolon. Man's cecum is normally carnivorous in type.

\*Shaler considers that the upright position more than any other single factor has fixed the short limits of man's life.

There are three deviations from the normal course of enteric development which are of great surgical interest. Rotation may fail; fixation may fail; the cecum may conform to the ancient herbivorous type. Any or all of these variants may, under pressure of gravity, produce areas of dilatation and atonicity which result in a slowing of the intestinal current, frequently ending in infection. Is it not easy to see that, given a cecum of this ill-adapted, pseudo-herbivorous type, it may undergo changes in the following sequence; stagnation, gas formation, dilatation, attenuation, infection, destruction of Auerbach's plexus? Barber has shown in recent animal experiments the important difference in the character and location of the dilatation following partial and complete obstruction. In brief, partial obstruction of the colon caused dilatation of the duodenum only, while complete obstruction caused contraction of that organ and colonic dilatation just oral to the obstruction. An analogy may be drawn between this process and that which destroys so many gall-bladders and appendices. The difference is that we have come to a recognition of the one, but not, as yet, of the other.

Bloodgood has observed a vast difference in the postoperative behavior of his colonic cancer cases and those in which the colon has been resected for other causes. There was a rapid restoration of function in the cancer cases, but when the colon was resected for other causes the return of function was slow and often incomplete. These observations accord with our own, and we consider the following to be a possible explanation.

The earliest sign of cancer is constipation. This occurs irrespective of the size of the growth or of its encroachment upon the gut lumen. It is equally true of laterally implanted growths, as of the an-

nular types. It is next to impossible, either by catharsis or enemata, to empty the bowel of the fecal mass which accumulates in the dilated pouch just oral to the growth. We have confirmed these observations repeatedly, especially in the case of minute recurrences which could not possibly in themselves offer any excuse for mechanical obstruction, the bowels having been regular since the primary resection and up to a short period before the recurrence. This inhibition is perhaps associated with Nature's effort to cause a recession of the growth. It is common practice to associate diarrhea with a new growth, but, of course, diarrhea is no evidence of the absence of constipation, for paradoxical as it may seem, the diarrheas most persistent are those associated with constipation. This frequent and imperative desire to defecate is not properly a diarrhea, but a mere subjective reflex without objective basis. So often is a diarrhea of this kind mistaken clinically, and so closely may it appear to be allied to the inflammatory conditions of the colon that one cannot consider them true inflammations without mentioning malignancy. We think it would be well to confirm or disprove our findings, that often the earliest clinical sign of cancer is a relatively sudden constipation.

In our studies we have noted that colonic infection appears to bear a measurable ratio to the degree of morphological variation from the normal occurring in the organ or in its mesentery. Furthermore, of the fifteen ceca removed and studied microscopically and found diseased as per the following reports, all showed inflammatory change. Of all the other cases in which developmental reconstruction was not done, but rather a simple colostomy or ileostomy, not one organ conformed to what is considered anatomically normal.

Infections of the colon vary from a mild catarrhal inflammation to the most severe involvement of the entire wall and the seroperitoneal fat. While as yet we can offer no conclusive evidence upon which to base a rigid classification of colonic infections, it is evident, clinically, that there is wide variation in the course pursued by the infection, in its position, its virulence, and its outcome. Some infections, and these are frequently seen in the infantile or fetal type of cecum, are confined more or less closely to the cecum and cecocolon. This may be because of the direct continuance here of the cecal and appendicular walls. Of this interesting relationship there is no direct proof, but a further series of observations might prove the hypothesis, namely, that the cecocolonic infection was primarily of appendicular origin. In discussing the origin of colonic infection our laboratory colleague, Dr. McFarland, suggested that here as elsewhere the hematogenous pathology of infection was deserving of careful consideration. The virulence is to be measured in terms of physical and mental systemic disturbance rather than in the amount of blood and mucous in the stools. Here, as elsewhere, the streptococcic infections are most serious, although in a woman who was completely disabled mentally and physically we have isolated a pure culture of colon bacillus from a gland found in the cecal mesentery.

The outcome of colonic infection is most interesting because of an apparent paradox. The virulence of the infection is no index of the degree of subsequent strictural deformity. The infections which usually result in stricture are comparatively mild. We have seen very severe streptococcic infections leave no deformity whatever.

CASE 259.—A railroad engineer. Clinically mild in-

fection; passing blood and mucous, but able throughout to run his engine. Proctoscope showed a colon inflamed in spots, which bled easily on the slightest touch, covered with mucoserum. No ulcers whatever. Sick for six years. Gradual narrowing of descending colon to complete obstruction under medical and incomplete surgical treatment. Cured by exclusion of entire descending colon which is permanently destroyed.

CASE 254.—A young society woman. Severe constitutional symptoms. Proctoscopy showed a sero-purulent exudate and some ulceration. Microscopic examination of colon revealed an acute hemorrhagic inflammation of all coats, including peritoneum and adjacent fat precisely like that of carbolic or arsenical poisoning. The *Streptococcus viridans* was recovered from the discharges. Nevertheless, after appropriate surgical treatment, although she had been medically treated for a year and a half previously without improvement, she has gained thirty-five pounds and, clinically, the bowel is functionally perfect.

These represent the end results of two extremes of colonic infection, and many cases approaching the mean, serve equally to support the hypothesis stated above.

The general indications for surgical intervention are to be sought and found only after a most exhaustive study of each individual patient. First to be considered are the grossly evident colonic lesions. Rare, but prominent among these in point of importance, is hemorrhagic colitis. This embraces the following conditions: Acute streptococcic embolic septic colitis; chronic torpid ulcerous, slowly progressive colitis; acute diphtheroid hemorrhagic colitis. These forms of colitis yield only to surgical therapeutics. It is evident that no good purpose can be served by partial removal, because the colon is, as a rule, diseased from the ileocecal valve to the anus, and no one would here think of extirpation. It is a curious fact and well worthy of note, that the infections terminate abruptly at the ileocecal valve. This occurs in spite of the fact that



since the terminal ileum and the cecocolon have a common embryological origin one would naturally expect them to be susceptible to like infections. For it is undoubtedly true of the ileocecal valve, as has been proven true of the ureterovesical, that its power of preventing so-called ascending infection is almost nil, the physiological function of the ureter being paramount. Our clinical observations on the Bauhinian valve all tend to show that this is equally true of the gut, for ileac involvement is extremely rare except the gut functions be impaired by bands or adhesions, and quite irrespective of the valvular patency. This view is at variance with that of those surgeons who operate for the sake of restoring the valve. Further research here is evidently necessary. Thus, it appears to the essayists to be as yet an open question whether the immunity enjoyed by the terminal ileum, though it be the embryological analogue of the cecocolon, is due to the change in chemical reaction, or, as with the ureter, to a protection afforded by its unimpaired physiological function.

Whatever the cause of so-called hemorrhagic colitis, one thing is certain: though the clinical pictures may be almost identical, the histological findings are absolutely different. Undoubtedly, the infections must be as varied as the microscopic pictures. Bacteriologists are helpless to aid the clinician in reaching a specific basis for classification, and until they find it possible to interpret the clinical findings in a scientific manner we cannot hope to reach a satisfactory classification, nor can we hope to treat these cases in any way other than by operation.

The histological findings in support of our premise are as follows:

The first case shows acute inflammation from

the mucosa to the peritoneum. No desquamation of epithelium or destruction of glands. Submucosa shows both acute and chronic inflammation. The muscularis in some places is normal and in others chronically inflamed, with entire absence of nerve tissue. The discharges in this case are foul smelling and dark brown. The peritoneal gut is much thickened and appears in the form of a dense fibrocellular membrane which is only loosely attached to the muscle. The appendix is the seat of acute purulent inflammation. The mucosa shows leucocytic exudate with blood and pus.

In the second case the mucosa differs in that it is very deeply congested and has the appearance of the mucosa of carbolic acid or arsenic poisoning. In all sections in this case the entire mucosa is covered by exudate and presents a picture of intense inflammation. The blood vessels are greatly distended, but there is no evidence of degeneration of epithelium. The submucosa exhibits both acute and chronic inflammation here, also blood-vessels are dilated and engorged with blood. The musculature shows some process of acute inflammation and the blood-vessels are engorged with leucocytes. There is exudate scattered through the submucosa. Tubercles can be demonstrated, but are not of tuberculous origin. There are several giant cells. A careful study of the nerve tissue fails to give any evidence of participation in the inflammatory process. The musculature shows evidence of acute inflammation and the peritoneum forms a dense fibrocellular membrane which is adherent to the muscle.

The third case presents exudate throughout, but most marked in the mucous peritoneal coats. The crypts of Lieberkühn have been entirely replaced by a round-celled exudate. Blood-vessels are abun-

dant and engorged with blood. They are very numerous on the free surface of the mucosa. Apparently there is total absence of submucosa, in consequence of which the exudate layer replacing the mucosa rests directly on the inner muscular coat. There is round-celled infiltration of the muscular coat. There is no change in the peritoneum in this case.

Having considered the hemorrhagic form in a special manner, because of its severity, rarity, high mortality, and exceptional import to surgery, we turn to the more frequent infections, local and general. There are all grades of infection varying from very severe to mild. Some are merely catarrhal manifestations of direct extensions. Note the colitis from adventitious bands, from recurrent injury by floating kidney, and from contiguous pus tubes and gall-bladders.

CASE 487.—A woman of 49. Abdominal tumor removed nine years ago. General complaint, pain, loss of strength during the last five years. Secondary complaint, constipation, alternating with diarrhea. Medical treatment futile. Operation, mesoventrad incision showed omentum thickened, twisted upon itself, and rotated from right to left so as to produce a partial hour-glass stomach and a triple kinked and twisted mid-transverse colon. It is well shown in the color photograph. Cessation of symptoms since operation, one year ago.

It is surprising how slight the physical basis may be in order to cause a disability out of all proportion to it. The following case is illustrative.

CASE 362.—Constant diarrhea, blood mucus, and tenesmus. Nausea and gastric symptoms so marked as to have deceived a very prominent stomach specialist who considered the lesion to be gastric ulcer, and who treated it as such for several years. Cured by the simple removal of a polypus from the sigmoid.

Time will not permit us to consider tuberculosis, syphilis, diverticulitis, and many other constitu-

tional and congenital conditions. Suffice to say, that all require surgical treatment, the technique and details of which are well known.

We wish to emphasize here particularly the surgical therapeusis of certain special forms of colitis which have given brilliant results in our hands and which we believe are not in general use. This therapy depends upon the following simple axioms. *A stoma situated anywhere but oral to all the inflammation is worse than useless. Colonic resection, to succeed, must be based upon surgical physiology.* Thus, the therapy under discussion consists in providing for one class of cases, rest; for the other, resection. A differential diagnosis to determine in what class a given case will fall may be established as follows:

What are the indications for ileostomy; what for colostomy, and what for resection? Acute purulent hemorrhagic and the acute purulent inflammations of the colon differ in this respect. The first is usually a general infection of the entire colon and rectum, ending in death under ordinary treatment. Prostration is profound, temperature high and irregular, and the anemia is severe and progressive. The discharges have a particularly foul odor, and the pain is cramp-like. There is no condition in the whole range of surgery more certain to yield a brilliant result if ileostomy is done in time. Appendicostomy and cecostomy will not cure; they are inadequate and are contraindicated because unphysiological. Their use in this type of case is unwarranted, and gives a striking example of meddling surgery.

Another rare condition previously treated by irrigations and medication and occasionally by colostomy, is multiple polyposis. Ileostomy is the proper therapy. This lesion we believe to be secondary

to an infection and the histological findings tend to support this view.

CASE 180.—Diarrhea alternating with constipation. Abdominal pain and tenderness. Frequent mucus and blood in stools. Illness began in summer of 1900 and from that time up to May, 1912, the patient had acute exacerbations with intervals of freedom. Bowel was studded with growths varying in size from small pimples to those three-quarters of an inch in length and one-half inch in diameter. They were so thick that it would be almost impossible to put the finger on the bowel without touching one. Mucous membrane granular in appearance and inflamed and covered with pus. Operation in May, 1912, ileostomy. Following this appetite improved and patient was able to eat anything without discomfort. Gradual gain in weight from 137 pounds at time of operation to 152 pounds one year later. At present (1915) weighs about 160 pounds. When last seen the bowel was normal and there was no presence of any of the growths, mucus, or blood.

CASE 254.—Chief complaint, epigastric pain, heart burn, diarrhea, foul smelling, dark brown discharge. Ileostomy and subsequent gain of 35 pounds. Patient danced all one winter with ileostomy opening and none of her friends suspected its existence. A year and a half after operation, cured. About six months have elapsed since opening was closed. Since then several examinations have been made for occult blood and the report has been negative on each occasion.

The causative relationship of infection to polypoidosis is further supported by the fact that after ileostomy the inflammation subsided and the tumors disappeared.

The third colonic lesion to which we have given special attention is a local infection of the cecocolon, a typhocolitis not extending far beyond the hepatic flexure, and giving systemic symptoms of profound auto-intoxication. These cover a wide field of human ailments and are familiar to all.

The indications for laparotomy in cases not yielding to colonic vaccines and other suitable forms of



medical therapeusis as described by Satterlee, are chronic intractable constipation or diarrhea plus the characteristic mental lesions, together with x-ray findings and often with snow crepitation over the cecum.

Resection is indicated if a non-fused, inflamed, thickened, dilated, infected cecum often with a mesentery studded with enlarged lymphatic glands is found. As yet we have not been able to decide positively upon resection until after laparotomy. As resection is a vague term, not indicative of any particular technique, we have suggested the term developmental reconstruction in a previous paper. This embodies the resection en masse of the terminal ileum, appendix, and cecocolon to the region of the middle colic artery. When completed, it places the ileocolic juncture in the position occupied before birth, which is the adult position in the dog and may, therefore, be termed "developmental." This operation carries a mortality which is far from negligible and has been practised by us only on individuals who have had years of unremitting, unavailing medical treatment and who were in every way unfit. Of a series of thirteen, 23.1 per cent. died, 46.2 per cent. were cured, 23.1 per cent. improved, and 7.7 per cent. not improved.

We have made several observations during the post-operative history following reconstruction, which have been of value to us and may be worthy of record. The first is, that reaction is apt to be severe in proportion to the amount of handling in the neighborhood of the second portion of the duodenum. We have, therefore, recently taken great pains to avoid this, considering that it may have something to do with the sympathetic ganglion and plexus known to exist there. Another observation is that reaction, if present, is apt to

be delayed until after the fiftieth hour. Still another is that at least one among our cured cases was unquestionably saved through the administration of autogenous vaccine by Dr. Satterlee.

We never use saline solution in the rectum, first, because it is contrary to the laws of osmosis; second, because the salt increases the patient's thirst, and third, because there may be a considerable toxic element in so large an amount of sodium chloride. We give forty to sixty drops per minute of tap water by rectum after the patient is returned to bed and continue as toleration may permit throughout the first week. We are convinced by experience that the rate of absorption of tap water is so rapid that no possible danger can exist from its use, and this is further supported by the experimental fact that the colonic wound is normally sealed within two hours after its closure.

The postoperative care following ileostomy or colostomy is exceedingly important. It means comfort or discomfort to the patient. In the first place, if possible, the bowel loop should not be opened until the fourth or fifth day after operation. The efficiency of a colostomy is to a great extent dependent on primary union of the wound; if this fails the patient may have a hernia superimposed on the colostomy, and this means discomfort and inefficiency. On account of cramplike pains and accumulation of gas, the patient is often so uncomfortable that it is imperative to open the bowel by some method in order to afford relief. On more than one occasion we have accomplished this by passing a small trocar and cannula and allowing the gas to pass out in this way. We have occasionally used a small number ten or eleven French catheter, and closed the bowel with a purse-string suture. This at times is very satisfactory. There is one impor-

tant feature connected with ileostomy which we have learned, and that is to anchor the ileum to the abdominal wall about ten centimeters orad to the proposed stoma. This prevents prolapse and inconvenience; also prevents its buckling against the other side of the bowel and permits it to pass into the cecum. The proper care of the skin and provision for enteric drainage are points not to be overlooked. An ointment of zinc oxide, having for its base lanolin, should be applied to the skin for a radius of about five centimeters from the stoma all around; over this some fine starch powder should be dusted. A collar of two or three thicknesses of gauze will serve further to protect the parts. A bag with the rubber container at right angles to the collar, such as is made by Tiemann and modified by Dr. Treby Lyon, one of our associates, serves as an emergency receptacle in case of leakage. This, however, is not to be expected, at any rate, not after the new function has been established. The use of a receptacle is not always necessary following a colostomy, but it is imperative following an ileostomy.

Although the readjustment of physiological balance after ileostomy, particularly in relation to the absorption of water, may take place slowly, it has come in due season in all of our cases. The stoma is not so efficient as after colostomy, but this is largely compensated for by the sticklike character of the movements and by the relative absence of gas of fecal odor. We wish to emphasize what we have already published, that the fear of post-operative discomfort both from colostomy and ileostomy is grossly exaggerated.

In conclusion, we wish to emphasize the most careful differentiation of all colonic inflammations, not alone as to character, so far as that be possible,

but particularly as to distribution. Some infections are general, others segmental; the therapeutics rests largely upon this, an ileostomy being indicated for the one, a colostomy or a developmental reconstruction for the other. Many segmental infections, unless surgically treated, even though relieved and apparently cured by medical treatment, invariably relapse. Cessation of symptoms for a time does not mean cure. Such infections almost invariably end in stricture, so its preventive treatment is the early recognition and surgical treatment of the cause. Whatever the nature of the primary infection, it always becomes mixed after a short time. This principle underlies the therapy of the colon just as thoroughly as it does that of the lungs.

Heredity and the upright position play important parts in colonic pathology, and sympathetic recognition of man's place in Nature is an important step in directing colonic therapy.

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## ANASTALSIS AND THE SURGICAL THERAPY OF THE COLON.<sup>1</sup>

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THE physiology and the surgery of the alimentary canal have become so reciprocally interdependent each alternately correcting the mistakes of the other and showing the way and the need for further research, that it is now idle for either of these branches of medicine to proceed to any conclusions which are not finally and carefully weighed in the scales of the other. Witness the immeasurable effect upon the recent surgery of the stomach by the check of physiology, particularly as regards the subject of so-called drainage and the indications for and against gastro-enterostomy, and, in the immediate present, the interesting reversal of this order of progress in the reconstruction by surgery of many preconceived and erroneous physiological notions regarding the function of the colon.

It is true that the effect of physiological pressure has been very slow in making itself felt, else there would be fewer individuals suffering from needless gastro-enterostomies, made by the "practical" surgeon in the bland assurance, as Walter Cannon says, that the human gut is a "system of rubber tubes conveniently arranged for splicing." The utter truth of this humorous view has long been a reproach to surgery, and the words of this gentle humorist have

<sup>1</sup> Since writing the above, the authors find that Dr. Horsley, of Richmond, in Jour. Amer. Med. Assoc., August 23, 1913, describes a method of interpolating the ileum, somewhat similar to that described in their article. Lardennois, of Paris (personal communication), in order to preserve the valve, transplants it with a portion of the cecum into the sigmoid.



rightly carried greater weight with American surgeons than all the tomes of his physiological predecessors.

Obedient to the law of reciprocal reaction, it now appears certain that surgery will presently return to physiology, in fair exchange for her correcting influences, certain dominant facts regarding the colon which have hitherto been inaccessible to physiological methods of research. It seems therefore that the long hoped for and elysian prospect of a physiologicicochemical control of all intestinal operations is no longer utopian, but actually at hand. Certain it is that the sooner there is complete and cordial coöperation between chemist, physiologist and surgeon, the better for the solution of the bewildering maze of gastro-enterocolonic problems, the very existence of which is only just beginning to be recognized. For no one man can be master of surgical technique and of physiological chemistry as well, and it is progressively evident that the modern surgeon has much to offer his laboratory colleagues in the way of hitherto inaccessible material.

The vicarious assumption of the function of one organ by another in close physiological relationship must be much more common than in usually supposed and it no doubt affords explanation of the question so frequently asked, as, for example, of the removal of an appendix or a gall-bladder, "How does the individual prosper without it?" Doubtless, all the vital functions having long since been taken over by allied organs or perhaps by organs heterologous in morphology if not in function, the loss, by surgical removal of the evident and mechanical functions, such as intermittent storage was not harmful to the economy.

While this compensatory power of the human economy is in many cases facultative, it may, on the other hand, as illustrated by the following case, be congenital in type. Lynch has reported<sup>2</sup> the amazing instance given to him by Professor Stockard of Cornell, of a human being who reached the age of forty years with only ninety-six inches of intestine from the stomach to the anus. The significant point in this case and which bears particularly upon the compensation problem under consideration was that the lumen of the gut was decreased as shown by actual measurements in almost precise proportion to the decrease in the length. This obviously represents an effort of nature to equalize the rate of absorption, and that this was actually achieved is shown by the fact that the individual never suffered any discomfort; was well nourished, and died of an intercurrent trouble without any suspicion of abnormality ever having been suggested.

An excellent operative illustration of the facultative type is probably to be found in the Author's Case No. 988 in which *gradual* intestinal obstruction from ileocecal valve carcinoma becoming

<sup>2</sup> June meeting of the New York Gastro-enterological Society, 1914.

complete, was tolerated for ten days, the toxic signs being minimized, whereas, after two months of re-established function, *acute* obstruction at the same point proved fatal in three days, the toxic signs being so fulminant as to cause suppression of liver function and consequent death.<sup>3</sup> Seen in this light, it may well be that such an organ as the colon, for example, may, in certain cases have so outlived its usefulness to the human economy by vicarious transfer of function as to quite justify its removal. Many of the authors' cases collectively illustrate this point. No. 180 specifically so, because after ileostomy formed movements showed immediately at the stoma, proving that the ileum previous to obstruction had already assumed one clonic function. That from birth on, it had no function save that of a catch basin as intimated by certain enthusiasts, seems harsh and crude—diametrically at variance with every law and precept of biology.

In studying the author's series of eight ileostomies it is easier to believe in the hypothesis of function transfer from colon to ileum than to presuppose that the colon never had any function save that of storing and distributing toxic material. The gross clinical observations on this series of ileostomies alone will be given, the laboratory studies being reserved for a later paper. In each patient there was a marked gain in weight, the fecal movements from the ileum were always solid and the reaction was always acid. What could offer a more direct reversion of the older teaching of the physiology of the ileum?

Consider this question of colonic therapy from another viewpoint. If the organ has a function vicariously transferred for the time, how can we be certain that after a restitution of normal conditions, there may not properly exist an impulse to restore to the colon whatever functions it may have parted with under stress of weather? Such functional restoration has been noted by Satterlee in studying a large number of cases of water trap stomach. It has been found by him little short of amazing to note the rejuvenation of the function of the gastric mucosa after surgical replacement of the organ, and this is particularly so because no gross morphological change was noted in the mucosa at time of operation.

Potential as these queries necessarily must be, they are given kinetic value by the fact that out of any number of persons undergoing total colonectomy a large proportion will die from the immediate effects of the operation. Whatever the vital function of the organ, it is therefore obviously better to retain it *in situ*, either in whole or, under certain conditions of duodenal dilatation as described by Bloodgood, in part; *provided that suitable provision be made for emptying the organ at its oral extremity*. It seems to the writers as inappropriate to speak of cecal "drainage" as of

<sup>3</sup> Draper-Schlutz, The Glycuronic Function of Liver in Intestinal Obstruction, Jour. Amer. Med. Assoc., September 26, 1914, vol. clxiii, p. 1079-1082.

stomach "drainage," since, as shown by one of them,<sup>4</sup> as well as by numerous Röntgen-ray observations, no drainage of the stomach occurs from its most dependent part, except when the organ be temporarily paralyzed, as in the dilatation of the last stages of pyloric obstruction, because the *emptying occurs directly in line with the peristaltic waves, and not at right angles to them.*

From a study of a considerable number of cases of chronic colonic constipation, the writers are convinced that there is a well defined group in which the constipation is due to preponderance of the anastaltic over the prostaltic colonic wave. This is easily shown by the rapid transfer of a bismuth enema from the rectum to the cecum and the return to the rectum of a portion of the mass—some remaining in the cecum—the round trip occupying about six to eight minutes. The haustral segmentations are not affected; the return to the rectum is slower than to the cecum: gradually the bulk of the mass accumulates in that organ, and the reciprocal movement ceases.<sup>5</sup>

If, as we believe, there is this form of anastaltic constipation associated with coloduodenal dilatation and insufficiency of the ascending colon, and which can be easily diagnosed by the Röntgen-ray, it is evidently due to aberrant physiology rather than to faulty morphology, placement, or other mechanical conditions, and must be treated by a physiological rather than morphological method.

Anastalsis is therefore necessarily a most important factor in colonic therapy, for all observers are agreed not only as to the frequent existence of the anastaltic wave throughout the colon but also as to its preponderance over the prostaltic wave in the group considered.

It is not yet agreed in what exact per cent. of cases this preponderance occurs, but it is assuredly so large as to constitute the most urgent problem yet to be solved in the operation of ileocolostomy. This is positively demonstrated, not alone by several of the authors' cases, but by the actual postoperative clinical findings of those surgeons who are doing this operation most frequently. Patterson asserts that fully 5 per cent. of ileosigmoidostomies require colectomy at a subsequent date because of the packing and progressive dilatation of the partially excluded and occluded segment. It has been shown by the studies of surgical physiologists<sup>6</sup> that a totally occluded bowel will fill to bursting with fecoid material in a very short time, and that incomplete exclusion results in the so-called "policeman club" dilatation which if untreated results in terminal perforation.

Now as it is well known, the small gut possesses normally but

<sup>4</sup> Draper, *Studies Surg. Lab. Columbia*, vol. i, 1907.

<sup>5</sup> Observations on author's cases by L. T. Le Wald.

<sup>6</sup> Brown Blake, *Studies on Exclusion. Studies from the Laboratory of Experimental Surgery*, Columbia University, vol. i, 1907.

one; the prostatic wave. Upon this fact is based two of the methods of surgical therapeusis outlined below.

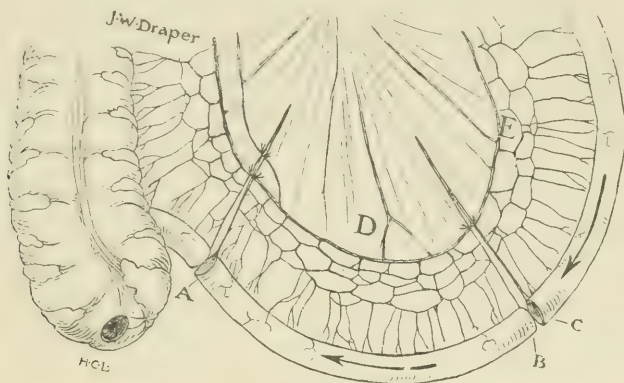


FIG. 1.—Ileo-ceco-sigmoidostomy. A new method of draining the colon with or without short-circuiting. The conditions calling for this physiological method of drainage are severe anastaltic constipation or cecal dilatation, secondary to previous ileo-sigmoidostomy. First stage in technique.

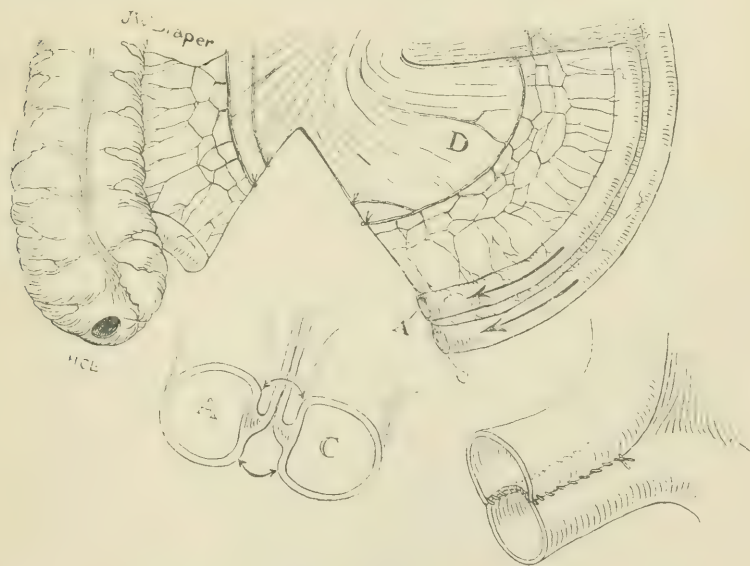


FIG. 2.—Ileo-ceco-sigmoidostomy. Second stage: The ileac segment *AB* has been slipped cephalad over *C*. This is done to facilitate the sewing of the ends *AC*, as shown in the detail sketches.

Draper (unpublished studies from the Mayo Laboratory of Surgical Chemistry and Physiology, Rochester, Minn.) has shown that circular segments of ileum may be transplanted into the colon without undergoing any gross morphological change. This



has also been demonstrated by others. In each of these instances, however, the transplant was designed to bridge a gap in the sigmoid following resection for malignant growth, the operators making no mention of the possible important physiological therapeusis of this procedure. It is evident, however, that such a ring of ileum would serve to block the colonic anastaltic wave and should prevent the return of material to the cecum. Halsted was the first to record experimental studies in gut reversal, and we know from his work, and from that of later observers that solid materials have a tendency to collect at certain points if the course of the waves is broken, and this tendency might or might not be a factor limiting the value of the blocking method suggested.

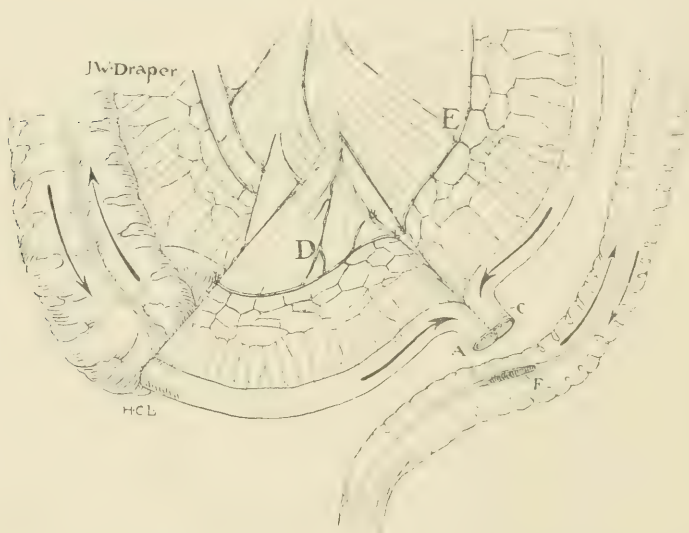


FIG. 3.—Ileo-ceco-sigmoidostomy. The cephalad end of the ileac segment has been united to the cecum and the double-barrel anastomosis with the sigmoid is about to be made. Note the predominant anastaltic wave in sigmoid as shown by arrows.

In the presence of a sufficiently strong wave there might therefore possibly be developed a tapering colonic dilatation immediately aboral to the transplant. This, however, does not occur in the author's experience with this procedure in animals.

The physiological hypothesis which should explain the failure of cecosigmoidostomy may perhaps be found in the fact that the current is distaltic or oscillating. Reasoning from this hypothesis the authors have resorted to the technique shown in Fig. 1, and the work has been done on animals and upon the cadaver. The ileac segment *B* which is made of proper length to reach comfortably from the cecum to the sigmoid, is slipped up on the ileum



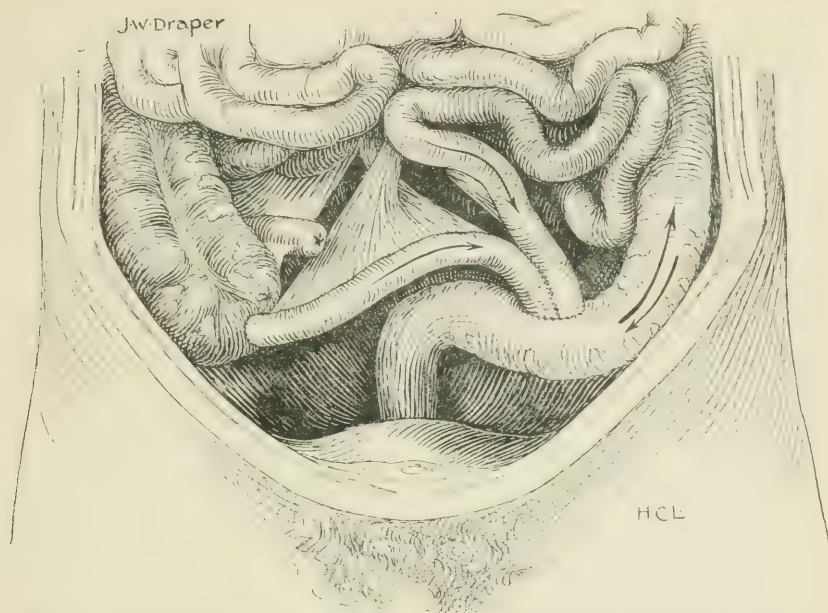


FIG. 4.—Ileo-ceco-sigmoidostomy. The operation is complete, with the exception of closing the ileac fossa.

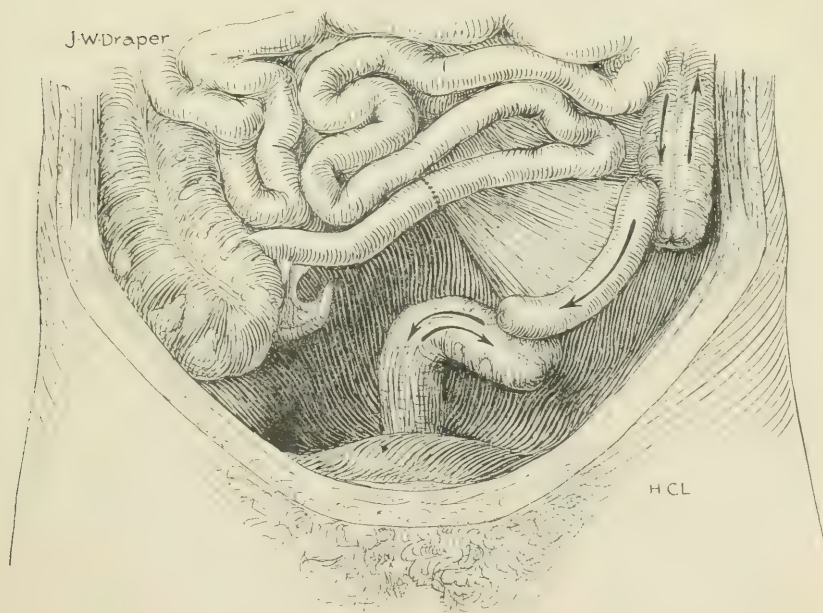


FIG. 5.—Anastaltic block. The monostaltic wave of the ileum is interposed to break the continuity of anastalsis.

and united throughout about half its length as shown. Terminally the aboral ends are sutured together so that a circle results. The effect of this technique is virtually the production of a double-barrel gun, and the end to side implantation into the sigmoid is thus converted into a single procedure. The oral extremity of the segment *B* is then inserted into the oral extremity of the cecum. Material is in this way able to pass from the cecum to the sigmoid, but cannot reverse its direction. The oscillating distaltic wave is made constant or monostaltic.

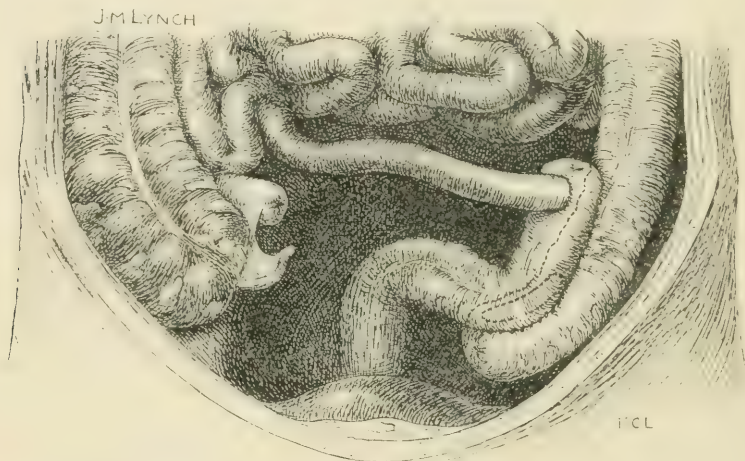


FIG. 6.—Ileo-sigmo-sigmoidostomy. Section and overlapping of sigmoid to block anastalsis. The cephalad current will not pass through the stoma.

Fig. 2 shows the physiological blocking of the anastaltic wave by the transplantation of the prostatic ileac segment. This procedure may be employed as an aid in preventing reflux after the usual operation of ileosigmoidostomy.

Fig. 3 shows a very simple method of preventing anastaltic reflux after ileosigmoidostomy. This operation is performed after the usual technique. After the anastomosis has been completed, the sigmoid is divided between clamps, and by means of a cautery immediately oral to the anastomosis. The aboral end of the sigmoid is invaginated after the usual manner, and the oral end slipped down beside the aboral limb until the oral extremity is several inches below the ileosigmoid anastomosis. The operation is completed by a termino-lateral anastomosis.

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## CHRONIC DILATATION OF THE STOMACH.\*

### A CLINICAL AND EXPERIMENTAL STUDY.

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DISTENTION<sup>1</sup> is a physiological increase in the size of the stomach. Acute dilatation<sup>2</sup> extends over a few days, and follows inflammations and injuries of the brain, nerves, or stomach muscle. Chronic dilatation is the end result of a gastric overload, and extends through a period of months and years. Fagge, in 1873, states, "Dilatation of the stomach, independent of obstruction at the pylorus or in the small intestine, is a condition which has long been recognized," and Mayo,<sup>3</sup> in 1903, reports twelve cases of chronic dilatation without obstruction.

Osler<sup>4</sup> considers the stomach "absolutely dilated" when the capacity exceeds Ewald's normal of 1600 c.c. Delay is frequently present. Indeed, Mayo considers the most valuable evidence of the test breakfast to be the presence or absence of raisins swallowed at the preceding evening meal. Prior to the introduction of the x-ray he had concluded

\*Read before Ex-Interne Society of M. E. (Seney) Hospital, March 25, 1915.

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that the retention of raisins over night was in certain cases ample justification for exploratory laparotomy. Nevertheless, laboratory studies of the gastric contents, especially when pursued by the fractional method,<sup>6</sup> are of scientific interest, if not often of confirmatory value. Of essential morphological value is the information obtained from an examination of a stomach section, if only of the seromuscular wall of the stomach, though it is recognized that opportunity for obtaining such material is infrequent. Properly series roentgenograms are of course of confirmatory value in defining the stomach and estimating its functions in terms of the bismuth meal. The *x*-ray standard fixes the intercrystal line in the dorsal prone and 4 cm. below that line in the upright positions as the caudal limit of extension of the greater curvature of the stomach, and allows six hours for discharging its contents into the intestines.\* Therefore, sag and inertia as detected through the *x*-ray are inferential evidence of increased load, or decreased prostaltic power. Finally three important symptoms in long standing cases are abnormal holding capacity, retention, and sag, any two of which, for general purposes are sufficient to make a most probable diagnosis of atonic dilatation.

Etiologically dilatation appears to be the primary equivalent of two opposing dynamic forces, namely, contractility and distention. On this basis any factor decreasing the prostaltic or increasing the resistant powers of the stomach is causal in chronic dilatation. Among such factors may be mentioned, on the one hand, prolonged toxemias and infection, general bodily overwork, insufficient nourishment,

\*Standard used at the Gastroenterological Clinic, N. Y. U.



and unhygienic surroundings; and on the other hand, habitual overeating and overdrinking, and mechanical obstruction. Glenard's gastropotosis and the water-trap stomach, recently described by Satterlee and LeWald,<sup>7</sup> by lengthening the pyloric arm and prolonging the exposure of the stomach wall to the toxic material, probably both retard and impair normal gastric emptying.

Huntington,<sup>8</sup> in his comparative anatomical studies, states "in animals whose bodies are long and slender, as in most saurians, many teleosts, the stomach is likewise usually long and slender in shape, unless special modifying conditions exist." This influence of shape and size of the abdominal cavity would therefore account for the vertical position of the adult human stomach, but its dilatation, according to the same author, is an acquired character, the resultant in part of the habitual amount of food required and the volume and digestibility of the food. This probably explains the incidence of gastric ptosis with dilatation in the individuals of two or more successive families. It has been strikingly illustrated to the author in the "M" family (referred to the author through kindness of Dr. B. P. Farrell), in whom the grandmother, two daughters and one grandson have been found to have dilated ptosed stomachs, and also in the "S" family (referred to the author through kindness of Dr. G. R. Satterlee), in whom mother and daughter were incapacitated for the same reasons.

Physiologically, therefore, dilatation appears to be the dynamic resultant of work and load, with the balance in favor of the load. Such a state is usually acquired, but often predisposed to by torsal malformations, which are apt to be accompanied by a vertical stomach.



TABLE NO. I—SHOWING EFFECTS OF ARTIFICIAL STENOSIS OF PYLORUS UPON STOMACH. (DILATATION, IN ITALICS, IMPLIES EXCESSIVE DILATATION)

Dog No.	Method of Raising Resistance to Gastric Emptying Used in Attempting Artificial Dilation of the Stomach	Days of Life	Gross Findings*
105	Resection of pyloric mucosa.....	5	Dilatation
159	Resection of pyloric mucosa.....	19	Dilatation
171	Resection of pyloric mucosa.....	12	<i>Dilatation</i>
111	Resection of pyloric mucosa.....	31	Dilatation
177	Resection of pyloric mucosa.....	42	Normal
160	Resection of pyloric mucosa and circumcision at pyloric incisure.....	37	<i>Dilatation</i>
131	Resection of pylorus.....	23	Dilatation
176	Resection of pylorus.....	42	Dilatation
170	Resection of pylorus.....	35	Dilatation
113	Resection of pylorus.....	30	<i>Dilatation</i>
175	Pyloric obstruction after Bartlett <sup>10</sup> .....	41	<i>Dilatation</i>
148	Artificial water-trap†.....	58	Hypertrophy
158	Artificial water-trap.....	14	Dilatation

Experimentally an attempt has been made to increase the pyloric resistance in thirteen dogs' stomachs, and study its effect upon each stomach wall after a certain lapse of time. The pyloric mucous outlet was resected one-half in eleven dogs and the pyloric arm lengthened twice by anchoring the stomach 8 cm. cephalad to the pelvic brim in two dogs. All were allowed to live from one to eight weeks before being submitted to gastroenterostomies. In each case but two the stomach was found dilated. These were a normal stomach and a stomach grossly hypertrophied and freed from its new attachments in caudad abdomen. The pylorus was found patent in each case. It was possible in several of the artificially stenosed cases, even though, as generally happened, firm adhesions were found about the pylorus, that the pyloric canal had regained normal size. In view of this overwork it

\*For Pathological Findings see text.

†Stomach had freed itself from its attachments and returned to normal position and size.

TABLE NO. II—SHOWING EFFECTS OF GASTRO-ENTEROSTOMIES UPON "DILATED STOMACHS. (PERCENTAGES WERE OBTAINED BY ESTIMATING THE CONTENTS OF THE PYLORIC AND STOMA LOOPS AFTER FEEDING MILK AND BEADS)

Dog No.	Duration of Plus Physiologic Resistance in Days	Location of Stoma	Emptying Per Cent. Through Pylorus	Through Stoma
194	0	"Pendant"	0	0
198	0	Pyloric antrum	0	0
111	31	"Pendant"	(Stomach contracted at necropsy)	
203	0	Pyloric antrum	54½	45½
205	0	"Pendant"	63	37
148	58	Pyloric antrum	34	35
		"Pendant"		31
170	35	Pyloric antrum	69	31
131	23	Pyloric antrum	(Stomach dilated at necropsy)	
113	30	"Pendant"	12	88
176	42	"Pendant"	(Stomach dilated at necropsy)	
177	42	Pyloric antrum	(Stomach contracted at necropsy)	
228	0	Pyloric antrum	Percentages not obtained. Greater amount of fluid resembling fluid found in stomach in loop from pylorus	
224	0	"Pendant"	Percentages not obtained. Greater amount of fluid resembling fluid found in stomach in loop from pylorus	
232	0	Pyloric antrum	80	20
226	0	Pyloric antrum	90.9	9.1
227	0	"Pendant"	99	1
242	0	Pyloric antrum	Stomach dilated. Most of milk curd found in loop from pylorus, less in loop from pyloric stoma, and least in loop from pendant stoma	
		"Pendant"		

appeared certain that at least a functional if not a structural change had occurred in the gastric wall, probably in the musculature, possibly in the elastic tissue, as suggested by Dr. Alexander Fraser. In each of the stomachs there were noted pallor and deficiency of blood supply, absence of rugæ, giving the stomach an ironed out appearance and thinned out walls. To date no constant muscular or elastic tissue change has been discovered microscopically in any of the above dogs' stomachs,

but retention of stagnant fluid and indigestible material have been frequently observed. Mayo-Robson,<sup>9</sup> on the other hand, speaking of the pathology of human dilated stomachs, gives: "(a) Degeneration of muscle (fatty, colloid), (b) want of nerve tone, or paresis, (c) organic disease of the muscle due to fibrosis." Therefore, it appears that a stomach may be clinically dilated and still show no pathological tissue change in its muscular fibers.

The treatment, as pointed out by Kaufman,<sup>1</sup> "will depend to a much greater extent on our ability to regulate the patient's mode of living and on the patient's ability to observe general hygienic and dietetic principles and rules, which consider not only his local disorder, but in the broadest possible way his constitutional make up, his mental state, his work, and his habits." Nevertheless, when this course fails, as it occasionally does for economic and other reasons, recourse may be had to surgery with some hope of hastening relief, if not recovery, from symptoms.

The surgical therapeutics of this affection appear to lack standardization. The methods pursued are as diverse as are the notions of the principles of its surgical physiology. Hence plication, suspension, or fixation, resection by knife, or suture, and gastroenterostomy have been recommended. W. J. Mayo<sup>3</sup> reports most success with plication combined with Finney's gastroduodenostomy. Mayo-Robson<sup>9</sup> favors gastroenterostomy alone. Gastroenterostomy seems best to meet the indications of relatively increased resistance or insufficient emptying power. It has been studied in the laboratory and in the light of experimental findings applied clinically.

Experimentally an effort has been made to study

the comparative efficiencies of pyloric and "pendant" stomata in gastroenterostomy for dilated stomach. To this end sixteen dogs have been used. Of this number seven underwent artificial pyloric obstruction for twenty-three to fifty-eight days. In each of fourteen posterior gastroduodenostomy was done. In two double posterior gastroenterostomies were performed. The stoma was made 3 cm. in diameter. Five to eight days later, under morphine-ether anesthesia, the loops at approximately equal distances aboral to pylorus and stoma, respectively, were loosely ligated with gauze. One day later the dogs were fed 30 c.c. milk. At the end of one hour each dog was killed and contents of the loops were weighed. Glass beads were substituted for milk and counted in a few animals. Resection instead of ligation was performed in four dogs.

From a study of Table No. 2 it appears that the pylorus is the most efficient outlet from the gastroenterostomized (or otherwise normal) dog's stomach, and that, other factors being normal, the closer the artificial opening coincides with the physiologic opening, the greater becomes its efficiency as a stomach outlet. However, of these factors, muscle tone is vitally important, and probably variable clinically, especially in instances where gastroenterostomy is indicated. Dog 113, Table No. 1, was noted as "dilated," and after a stoma was placed most suitable for "pendant drainage" it became 88 per cent. efficient. This was not true, however, of dog 205, with a previously normal stomach, whose "pendant" stoma was but 37 per cent. efficient.<sup>12</sup> In each case in which double gastroenterostomy had been performed acute dilatation was found; the character of the intestinal contents, how-

ever, indicated that over two-thirds of the stomach contents left the stomach after passing through the pyloric antrum.



FIG. 1.—Case I.

Clinically two human cases are typically noteworthy; one a recurrent total failure under medical treatment, and the other a comparative failure from



prolonged medical treatment and a Coffey suspension operation.

CASE I.—J. L., age 28. Symptoms for eight years.



FIG. 2.—Case I.

Complained of constant pain in the pit of his stomach, without reference to eating. He has *eaten* bicarbonate of soda, vomited, and in this way relieved "heaviness" in stomach, two or three times a week for the past

year. Said he vomited one or more quarts, and noticed remnants of food eaten one or two days before. Headache and constipation. Lost eight pounds in six months. Negative Wassermann. Had been treated

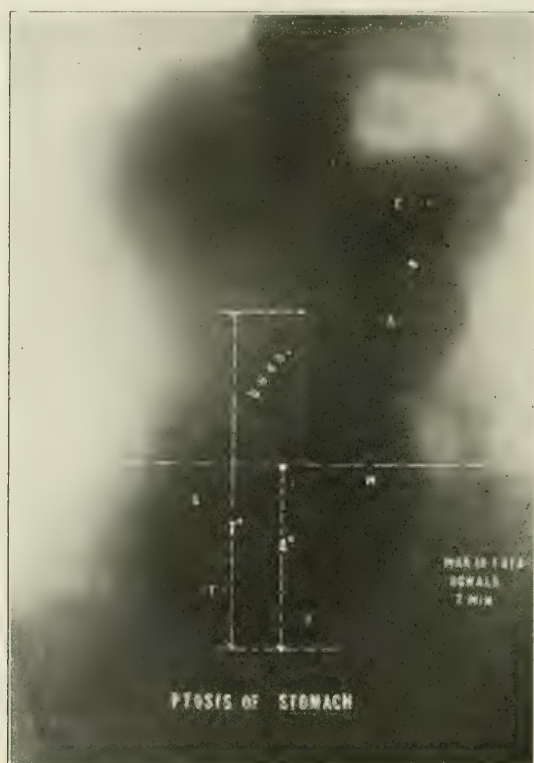


FIG. 3.—Case II.

medically for the past two years, with three recurrences. Signs were those of gastrocoloptosis. X-ray

(Fig. 1) showed marked sag, increased size, and retention of the stomach. Was operated upon October 19, 1914. Appendix pale and atrophic, removed, stomach large and thin-walled. Posterior gastroenterostomy



FIG. 4.—Case II.

performed with stoma in pyloric antrum. No ulcerated area was actually seen but the pylorus seemed to

be the site of induration, because it barely admitted the tip of the index finger.

November 13, 1914. Entirely free from pain. Has much gas and stomach feels "heavy." Occasional

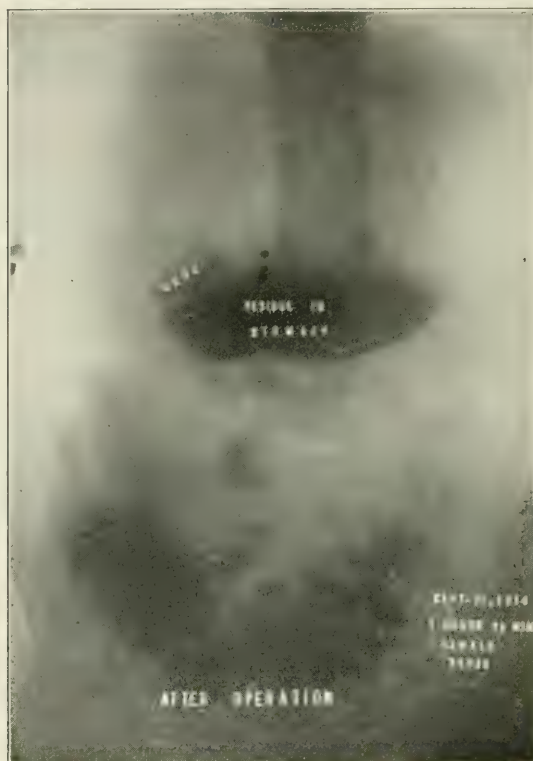


FIG. 5.—Case II.

headache, less constipated. Vomiting less. January, 1915. Reports free from pain, heaviness and vomiting.

CASE II.—J. O., woman, age 47. Had symptoms for twenty years. Complained of pain and heaviness in epigastrium, relieved by vomiting, which she brought on at least twice a week. Insomnia, headache, constipation, and loss of weight.

She had a narrow subcostal angle with ptosed stomach, liver and kidneys; urine and feces negative. Roentgenogram, as illustrated, showed ptosis of the stomach and delayed emptying. Was treated medically without any appreciable improvement for months.

March 30, 1914. A chronically inflamed appendix was removed, a Jackson's veil divided, pyloroplasty and a Coffey suspension operations were performed. The plastic was done not to widen the pylorus, but to allay the suspicion of ulcer at the pylorus. The pylorus was contracted so as to admit but the tip of the index finger, and the walled up mucosa, as in previous case, gave sensation of indurated area. Not only was the pyloric opening perfectly smooth when felt through the incision and the pylorus itself relaxed to three fingers,\* but the section removed from the suspected area was absolutely negative. This patient was carefully followed for the next nine months. Although she gained eighteen pounds and felt generally improved she was not free from headache, constipation and occasional nausea. Roentgenograms showed stomach up, but with residue. January 11, 1915, gastroenterostomy was performed with "pendant" stoma. The result to date has been all that could be looked for. Taste and appetite have returned for the first time in over ten years. The metallic taste has disappeared. She eats everything, and has gained seven pounds in the first week from the hospital. Bowels move freely twice a day without cathartic. Insomnia has entirely disappeared.

From a review of these cases it appears that medical treatment alone as well as medical treatment assisted by suspension were inadequate for the complete symptomatic relief of these chronically

\*Complete pyloric relaxation following marked stenosis has been noticed in stomachs of dogs under deep narcosis. The difficulty of deciding positively on duodenal ulcer even on the operating table, is well shown in these two clinical cases.



dilated and atonic stomachs; that gastroenterostomy secured at least to date this relief, which was gradual (three months), with the stoma in the pyloric antrum, and immediate (three weeks) with the opening in the "pendant" stomach. Regeneration of the atonic musculatures is questionable, and what effect such a stomach improvement may continue to have on the comparative efficiency of the two artificial stomata remains to be proved.

"One understands," writes Professor Hartmann," "that the juxtapyloric anastomosis works actively when the pylorus is normal, and that the anastomosis in the cardiac part is functionless in cases of permeable pylorus." It appears, however, that a "pendant" stoma works actively in the presence of a permeable pylorus when the stomach is dilated, or its muscle-emptying power is pathologic. Dilatation undoubtedly occasionally exists where gastroenterostomy is indicated, and should, of course, be carefully estimated before placing the stoma. Pendant drainage in presumably pathologic stomachs is well illustrated by A. Ogarkow,<sup>14</sup> who compared the dried stomach residues removed by stomach tubes after submitting the patients to various postures. He found 19.5 per cent. of the test breakfast remaining in the stomach after an hour's lying on the right side, while in the prone and upright positions for the same time it rose to from 25-34 per cent. Similarly Jefferson,<sup>15</sup> in studying the *Canalis Gastricus* in the human stomach noted that when bismuth cream enters the stomach it is confined to the lesser curvature in 82 per cent. and in 18 per cent. "it spread rapidly over the sides of the stomach." "These stomachs," he observed, "were atonic, though healthy—a combination by no means rare." The importance of gravity on gastric emptying in re-

spect to the dilated and atonic stomachs must therefore be reckoned with medically, and in those few cases in which surgical aid is sought it should influence the localization of the stoma.

*Conclusions.*—1. Chronic atonic dilatation, etiologically and therapeutically considered, is a problem in pathological physiology.

2. Most cases are amenable to medical treatment. Many are relieved by suspensions. Of both of these classes many are entirely correctable physiologically by carefully planned gastroenterostomies.

3. The position of the stoma is vitally important and depends on the following: (a) For normal or hypertrophied stomachs the pylorus is the most efficient outlet. (b) For normal or hypertrophied stomachs the nearer the artificial stoma corresponds with the physiologic point of outlet the greater is the efficiency. (c) For "moderately" atonic stomachs or stomachs with 50 per cent. impaired peristaltic power, the efficiency of the stoma is probably greatest in the pyloric antrum, while (d) for the markedly atonic stomachs, with pronounced muscular insufficiency, the pendant stoma seems to date most efficient.

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# DILATATION OF THE DUODENUM

AN EXPERIMENTAL STUDY \*

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THE coincidence of dilatation of the duodenum and ileac retention is frequently recognized in X-ray studies on gastro-intestinal cases. At operation a dilated duodenum is often found associated with a constriction or angulation or otherwise contracted caudad ileum. These observations<sup>1</sup> have been frequently made by clinical gastro-enterologists apparently without attempting to explain any dynamic correlationship between the muscular or neuromuscular tone of the duodenum and that of the aboral ileum.

Experimentally the problem has presented itself: is there not some causative interplay between incomplete obstruction of the extreme caudad ileum and dilatation of the duodenum? It is commonly known that constipation, long continued, may terminally present the aspects of cæcal stasis. In laboratory terms it is the author's experience that experimentally produced constipation in dogs is followed by the dilated atonic cæcum. In other words, incomplete obstruction of the caudad colon is associated with dilatation and increased dilatability of the cephalad colon. An analogous association has been observed in the ureter.<sup>2</sup> Is there not some functional interdependence of the muscular states of the two ends of the small intestine?

Ochsner's anatomical studies have revealed a concentration of the circular fibres of the duodenum 2.4 cm. aboral to the entrance of the common bile duct. He holds that this "duodenal sphincter" may work in concert with the ileocæcal valve and the pylorus: that an appendicitis stimulates the closure of the ileocæcal valve, giving rise to ileac retention, to closure of the duodenal sphincters, thus favoring duodenal ulcer, to pyloric closure—thus interfering with the normal progress of food.<sup>3</sup> It is significant that in this study, dilatation of the duodenum has been found invariably greatest in the portion cephalad of the common bile duct.

Mr. Lane,<sup>4</sup> on the other hand, explains duodenal dilatation on a mechanical basis, thus, "The accumulation of material in a large pro-

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lapsed cæcum" may result in ileac delay and accumulation. Or obstruction of the ileum may be still further exaggerated by an "ileal kink" or by a "fixation of the appendix to the under surface of the mesentery by adhesions." "The *accumulation of the material in the small intestine* drags upon and obstructs the duodenojejunal junction. In consequence the duodenum is elongated and dilated and especially in its first portion where it is free and surrounded by peritoneum." Both authors therefore agree in the importance of ileac retention as a factor in duodenal dilatation, but differ in the mechanism of retention; the former mentioning reflex closure of the ileocæcal valve from appendicular irritation; the latter holding to mechanical interference with the lumen of terminal ileum.

Bloodgood<sup>5</sup> differs from the preceding authors in applying mechanical pressure at the point of dilatation. This is described under the capita: (1) Acute gastromesenteric ileus; (2) chronic gastromesenteric ileus, and (3) filling of the duodenal stump after gastro-enterostomy. With this contention Draper,<sup>6</sup> speaking from the stand-point of the Surgical Laboratory at that time, agreed, declaring that "dilatation does not occur in any organ except at the point of obstruction." The dilatation of the first and second portions of the duodenum were believed due to obstruction of the third portion. That the mesentery may exert such pressure has been doubted by Lynch<sup>7</sup> and others. That the pressure presumably exerted may affect an immediate dilatation depends upon the amount of pressure. The obstruction if incomplete must be greater than the potential peristalsis of the duodenum, as appears from experiments on the caudad ileum. Apropos of this dilatating load, Keilty and Smith,<sup>8</sup> in their recent review of 100 human autopsies, express themselves as follows: Stasis "is brought about by rapid reduction of the lumen of the gut without establishment of compensation or with compensation but with increased load producing fatigue and dilatation." Filling of the duodenal stump has been repeatedly observed experimentally. Occasionally this filling may be due to the relation of the oral duodenal loop to the stomach wave.

Dog 224; mongrel; female. Small intestine divided at caudad end of the oral third. Caudad two-thirds were anastomosed at mid-point, with antrum pylori placing stoma parallel with the greater curvature. Five days later greater amount of stomach test-meal that had passed through stoma traced into oral segment; opening into distal segment patent.

Dog 232; mongrel; male. Small intestine divided at same point. Caudad segment 5 cm. aborally anastomosed laterally in same manner to antrum pylori. A" test substances that passed through the pyloric stoma found in duodenal stump; opening into distal segment patent.<sup>9</sup>



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Should the passage into the jejunal segment be occluded certainly the contents of the duodenal segment must be so much the more increased. Hence it appears a pathologic load applied directly to the duodenum by a tensely drawn mesentery or the over-filling of the duodenal stump following gastro-enterostomy by the peristaltic stomach wave may dilate the proximal duodenum.

Christian<sup>10</sup> quoted Ochsner and Bloodgood and assumed duodenal atrophy to be associated in some way with gastric atony and pyloric relaxation.

It is generally agreed that mechanical obstruction [understood to be qualified as above described; this virtually amounts to a complete physiological obstruction] of the duodenum may give rise to immediate duodenal dilatation and that incomplete mechanical obstruction of the extreme caudad ileum from adhesions incident to appendicitis or surgical stasis is *occasionally coexistent with* mediate dilatation of the duodenum.

A number of animal experiments have been performed to determine a possible causative relationship of incomplete caudad ileac obstruction to dilatation of the duodenum. The ileum, 3 cm. from the ileocolic junction, was loosely ligated with gauze, so that the resultant potential lumen of the ileum within the gauze was equal to the lumen of the relaxed ileum. In a few of the animals a segment of ileum 8-10 cm. cephalad of the ligature was demarcated by a linen suture run through the seromuscular wall and loosely tied. A duodenal segment of equal length in every dog was defined by a similar suture an equal distance caudad of the pylorus. In order to decide definitely on the presence or absence of dilatation in all the latter dogs, each loop was injected with water from a 2 c.c. syringe, with intermuscular needle, until the injecta reappeared at the detached end of the needle on disconnecting the syringe. The ends of the outlined loops were compressed digitally during the filling of the segments. The amount of injected fluid was taken as a measure of the potential size or dilatability of each intestinal segment at the time of distention.

Dog No. 19; bull; male. October 29, 1914: Ileum compressed by gauze strip, 2 cm. in width; sutured end-to-end and, snugly, about walls of ileum 2 cm. from ileocolic junction.

November 5, 1914: Dilatation of duodenum for cephalad 12 cm.

Dog No. 112; mongrel; male. December 3, 1914: Caudad ileum compressed by gauze in similar manner.

December 9, 1914: Was operated upon for other reasons, and duodenum was noted dilated.

Dog No. 131; mongrel; female. December 10, 1914: Terminal ileum incom-

pletely resected for 2 cm. and reconstructed with a diameter of one-half original size.

January 17, 1915: Marked dilatation of duodenum.

Dog No. 149; mongrel; male. February 4, 1915: Caudal ileum ligated by moistened gauze strip so that resulting lumen measured approximately 1 cm. in diameter. Duodenum defined 10 cm. caudad by a linen seromuscular suture. Dilatability 14 c.c.

February 9, 1915: Duodenum dilated. Dilatability 19 c.c. Stomach contracted, colon dilated.

February 13, 1915: Duodenum dilated for 15 cm. caudad of pylorus. Dilatability 24 c.c.

Dog 179; mongrel; male. February 4, 1915: Caudal ileum obstructed incompletely by gauze band. Duodenum defined at arbitrary caudal plane by linen suture. Duodenum dilated. Stomach small. Dilatability 10 c.c.

February 9, 1915: Duodenal dilatability 22 c.c.

February 16, 1915: Duodenum buried in adhesions, freed, and admitted but 9 c.c. Adhesions undoubtedly interfered with further dilatability.

Dog No. 223; mongrel; female. March 9, 1915: Caudal ileum ligated with gauze strip; 8 cm. cephalad of ligature defining suture of linen inserted. An equal segment of duodenum similarly defined. Dilatability of ileal segment 10 c.c., duodenal segment 14 c.c.

March 18, 1915: Ileum cephalad of gauze ligature impacted with feces for 10 cm., which converted the incomplete into a complete ileac obstruction. Under this condition dilatability of duodenum was 6 c.c. and of ileum 60 c.c.

Dog No. 251; mongrel; male. March 27, 1915: Extreme caudal ileum ligated with gauze, without encroaching upon lumen of gut as found in relaxed state. Duodenal and ileac segments defined as above. Dilatability of duodenal segment 9 c.c. and of ileac 6 c.c.

April 1, 1915: Ileac loop contained small amount of pasty fecal material cephalad of ligature. This was emptied before injection. The apparent dilatation of either loop was negligible. Dilatability of duodenal segment 10 c.c.; of ileum 8 c.c.

Dog No. 252; mongrel; male. March 27, 1915. Similarly treated. Animal had mucopurulent nasal discharge and tonicity of intestine appeared very low. Ileum ruptured longitudinally while being injected. Died 36 hours later of pneumonia. Dilatability of duodenum on March 27 14 c.c.; of ileum 12 c.c. At autopsy duodenum showed no change.

Dog No. 259; mongrel; male. April 1, 1915. Similarly treated. Dilatability of duodenum 14 c.c.; of ileum 8 c.c. (loops of unequal lengths).

April 6, 1915: Duodenum dilated by inspection, dilatability 20 c.c.

Ileum enveloped in adhesions not dilated and ruptured when injected to capacity of 14 c.c. Gauze removed.

April 8, 1915: Duodenum appeared more dilated, but held 12 c.c. only. Ileum showed productive inflammatory change; held 3 c.c.

Dog No. 260; mongrel; female. April 1, 1915: Used as control. No obstruction but loops demarcated and injected.

Duodenal dilatability 10 c.c.; ileac dilatability 8 c.c.

Marked contraction of distended ileac segment followed immediately upon

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release of distention. A contractile wave appeared subsequently in cæcum and cephalad colon.

April 6, 1915: Ileocolic intussusception found and released. Under these conditions duodenum was noted not dilated and capacity found to be as above, 10 c.c. *Completely obstructing ligature placed about ileum cephalad of injured portion.*

April 8, 1915: Duodenum *apparently* dilated greatest at region of common bile duct entrance and traceable to 2 cm. caudad. Dilatability only 4 c.c. Ileum seriously damaged and impacted for 10 cm. cephalad to ligature.

Dog No. 264; fox terrier; male. April 6, 1914: Incompletely obstructed at terminal ileum 2 cm. cephalad of ileocolic junction. Dilatability of duodenum 10 c.c.; of ileum 10 c.c.

April 13, 1915: Adhesions about defining sutures. Ileum kinked by omental adhesions. Duodenum *contracted*, capacity 4 c.c. Ileum unchanged.

Dog No. 265. April 6, 1915: Control treated in the same manner with the omission of obstructing ileac ligature. Dilatability of duodenum 18 c.c.; of ileum 8 c.c.

April 13, 1915: Duodenum and ileum grossly unchanged. Dilatability of duodenum 10 c.c.; of ileum 6 c.c. *Completely obstructing ligature placed about caudad ileum.*

April 15, 1915: Duodenum contracted. Dilatability 6 c.c.

To determine a possible causative relation of cæcal stasis to dilatation of the duodenum as suggested by Lane, the following experiment was performed:

Dog No. 266; mongrel; male. April 8, 1915: Colon 2 cm. caudad of ileocolic junction ligated loosely, leaving potential lumen 1 cm. Duodenal segment defined and found dilatable to 14 c.c.; cæcum dilatable to 12 c.c.

April 13, 1915: Duodenum unchanged, held 12 c.c. Cæcum not grossly changed, held 8 c.c. *Completely obstructing ligature placed about terminal ileum.*

April 15, 1915: Duodenum contracted, held 6 c.c. Colon distended with gas and dried fæces.

To determine the possible causative dilatation of duodenum by appendicitis, the following experiment was performed:

Dog No. 267. April 8, 1915: The cæcum of the dog, similar in many respects to the occasional funnel-shaped human cæco-appendix, was injected with an emulsion of another dog's fæces and firmly ligated 5 cm. cephalad of tip. Duodenal loop defined and injected to 14 c.c.

April 13, 1915: Ruptured gangrenous cæcum and diffuse purulent peritonitis. Stomach unchanged. Duodenum unchanged, dilatability 8 c.c. Caudad ileum unobstructed.

Under the conditions of the foregoing experiments the following observations therefore have been made:

(1) Incomplete obstruction of the extreme caudad ileum gives rise to dilatation and increased dilatability of the cephalad duodenum.

(2) Complete obstruction of the extreme caudad ileum gives rise to no apparent change and decreased dilatability (or perhaps increased tonicity) of the cephalad duodenum.

(3) Incomplete obstruction of the cephalad colon or purulent typhlitis gives rise to no apparent change and decreased dilatability of the cephalad duodenum.

The researches of Alvarez,<sup>11</sup> Gerlach,<sup>12</sup> and Biedermann<sup>13</sup> have contributed certain important data bearing upon the relations of the duodenum with the caudad ileum. Alvarez made the following significant observation from his studies on intestinal segments of rabbits: "In removing the segments it was found best to begin at the

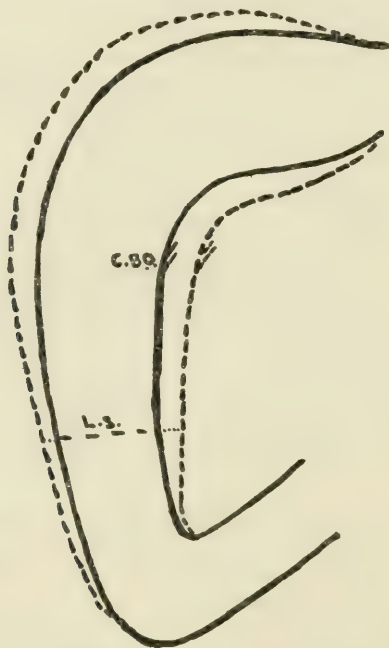


FIG. 1.—Diagram representing normal duodenum in full, and dilated duodenum in broken, line. In experiments presented the duodenum of mean volume of 12.2 c.c. dilates to a mean volume of 19.2 c.c. in 5.8 days, following a fixed potential diameter of caudad ileum of approximately 1 cm. (or incomplete obstruction). C. B. D., common bile duct; L. S., limiting suture.

pylorus and to proceed downward, as the bowels soon became distended and atonic after ligation of the ileum. When this happened segments from the duodenum did not beat well—the amplitude was poor, the rhythm was irregular, and fatigue appeared early." Gerlach has found considerable variation in the thickness of Auerbach's plexus in different parts of the intestinal tract. In the first 5–6 cm. of the duodenum he observed the largest fibres intermingled with the greatest number of ganglion cells. Below this point, which possibly corresponds with the site of Ochsner's "duodenal sphincter," the fibres gradually lost their



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cells and the meshwork became wider. Upon this nerve-net, according to Biedermann,<sup>15</sup> depend the rhythm and size of the peristaltic waves.

The whole neuromuscular arrangement appears quite analogous to that described for the ureter by Bardeleben,<sup>14</sup> and no doubt furnishes adequate anatomical explanation for the analogous physiological mechanisms of the small intestine and the ureter.

It is extremely difficult and hazardous to correlate all this experimental and anatomical material. It is evident, however, that an incom-

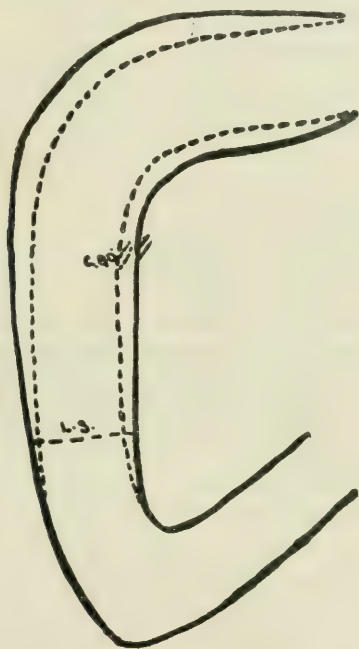


FIG. 2.—Diagram representing normal duodenum in full, and contracted duodenum in broken line. In experiments presented, duodenum of mean volume of 14 c.c. contracts to a mean volume of 6.25 c.c. in 5 days following a fixed potential diameter of caudad ileum of 0 (or complete) obstruction. C. B. D., common bile duct; L. S., limiting suture.

plete obstruction permits the free intercommunication of the duodenal and caecal centres through Auerbach's plexus, whereas a complete obstruction interferes with such relationship. Furthermore abnormal caecal stimuli, whether from an inflammatory appendix or an incompletely obstructed caecum, may have the same cumulative effect upon a duodenal centre as does the abolition of all such stimuli together. In other words, we should expect in the first case (incomplete ileac obstruction) a duodenum laboring to the points of fatigue and dilatation under



a plus physiologic load, and in the latter case (complete ileac obstruction, incomplete cæcal obstruction, and typhlitis) a conservation of duodenal contractile power and a more tonic duodenum.

The author is indebted to Prof. G. S. Huntington for his constructive criticism of this paper.

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**SPINA BIFIDA**

AN EXPERIMENTAL AND CLINICAL STUDY

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(Published from the Laboratory of Experimental Physiological Surgery of New York University and Bellevue Hospital Medical College)

SPINA BIFIDA, that curious congenital anomaly, has from time to time for many years engaged the attention of surgeons and embryologists. As yet the cause or causes of this condition are still unproved. The majority of embryologists unite in declaring that the chief factor, if not the only one, is a failure of the mesoblastic plates, in which the bony laminæ of the spine are developed, to close over the spinal canal, thus leaving a gap or defect. This lack of development they regard as the primary causative factor of spina bifida. In opposition to this theory the suggestion has been advanced at different times, usually by surgeons, that the lack of development of the mesoblastic tissues is not the primary cause, but is secondary—is a result. They suggested that the primary, or inciting factor, is an abnormal accumulation of cerebrospinal fluid, in early fetal life, which by exerting pressure prevents the coming together of the mesoblastic plates containing the rudimentary laminæ, in this manner producing a gap or defect in the spinal canal.

Several other theories have been advanced, none of which have received much support. They will be mentioned later.

The adherents of the first theory have advanced facts, marshalled arguments and presented the results of many experiments in their efforts to find the causative factor. But this is not yet definitely settled. The writer is one of those who believe that the second theory mentioned is the true one—that is, that the primary cause of spina bifida is the excessive pressure exerted by an abnormal amount of cerebrospinal fluid, this pressure preventing the closure of the bony laminæ. And he believes that the results of later experiments are tending more and more strongly to throw the weight of evidence in favor of this theory.

It is proposed in this article to discuss the various theories of spina bifida, to give the results of experiments in connection with this subject carried out by the writer in the Laboratory of Experimental Surgery of New York University and Bellevue Hospital Medical College, besides a short review of the different varieties of spina bifida with their symptoms, diagnosis and treatment.

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ETIOLOGY.—In view of the difficulties confronting the experimenter, in that spina bifida originates in early fetal life, and that it is impossible to confirm on a human subject the results of experiments on the lower vertebrates, it is unlikely that the cause of this curious condition will be found directly through experiments.

Of the various theories that have been put forward concerning the cause or causes of spina bifida, those which have received but slight support will be discussed first.

*Amniotic Adhesions.*—According to those who put forward this theory, the amnion becomes adherent to certain points along the dorsal ridge, and by traction prevents the mesoblastic tissues from crossing over and covering in the medullary groove. It is not explained how the amniotic bands selected the lumbosacral region, where by far the greater number of spinal defects are found. Besides, Dareste<sup>1</sup> and many others have, by chemical means, produced spina bifida in the embryos of amphibians, and these have no amnion. Mall<sup>2</sup> asserts that amniotic adhesions are the results of malformations, and not the cause of them.

Another theory advanced is that a *tumor* in the central canal of the cord, or in the spinal canal, in early fetal life, by its mere presence, prevented the laminae from coming together and closing the canal. Tumor masses, especially lipoma, are frequently found in the cleft in spina bifida occulta, but almost never in the other forms of spina bifida. Nor does this theory explain rhachischisis, and it has been given but slight support.

According to another theory, *kyphosis* of the spine, caused by exaggerated curvatures of the fetal vertebral column, so interferes with the development of the cord that spina bifida is the result. But as these exaggerated curvatures occur usually in the cervical and dorsal regions, it does not account for the majority of spina bifidae being found in the lumbar and sacral regions. Neither does it explain spina bifida anterior, nor the fact that the cord in a great number of cases is fully developed.

The theory that has received the greatest support up to the present, especially from embryologists, is that spina bifida is due merely to lack of development of the mesoblastic tissues that cover in the medullary groove.

The Committee on Spina Bifida of the London Clinical Society in 1885<sup>3</sup> stated: "The theory which best explains the pathological anatomy of spina bifida is that which assumes a primary defect of development of the mesoblast from which the structures closing in the vertebral furrow are developed. After the closure of the neural furrow it would appear that the processes of mesoblast which subsequently insinuate themselves between the primitive spinal cord and

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its overlying epiblast are formed in an insufficient degree to meet and combine, or that these processes, should they meet, are not formed in sufficient proportion to serve as a basis, from which the various structures subsequently to be produced over the spinal cord can be developed." This theory, in the main, is supported by embryologists, being merely modified in some respects by the results of experimentation. Bailey and Miller<sup>4</sup> say that "at the present time it is generally agreed that spina bifida is closely related to defective closure of the neural tube, although the exact nature of this relation is not known."

Hertwig<sup>5</sup> showed that if the eggs of axolotl are treated with a 0.7 per cent. solution of sodium chloride, all the embryos will have spina bifida; and Morgan and Tsuda,<sup>6</sup> by putting frog embryos in the early stages into a 0.6 per cent. solution of sodium chloride, produced spina bifida.

Recently some embryologists are abandoning the idea that spina bifida is due to lack of development of the mesoblast; to a germinal defect. They state that these experiments indicate that malformations are due to external influences, and not to defects in the germ itself. Mall says that malformations are not due to poisons in the maternal blood (corresponding to chemicals used in experiments) or to germinal defects, but to faulty implantation of the ovum in the uterine mucosa, or to an unhealthy condition of the mucosa.

In opposition to these theories, from time to time the opinion was advanced, mostly by surgeons, that the primary cause of spina bifida was some disorder of the cerebrospinal fluid circulation. But owing to the former scanty knowledge of the formation and outgo of this fluid, progress in this direction was hampered. Recent investigations in this field, however, have opened up this subject widely. We now know that the cerebrospinal fluid is a secretion, and not an exudation, and that it is formed by the choroid plexuses of the lateral ventricles. The remarkable work of Dandy<sup>7</sup> in stopping the outflow of fluid from the ventricles by plugging the iter, and injecting solutions of phenolsulphonephthalein into the ventricles, and in other cases into the subarachnoid space, and timing its appearance in the urine, shows that the cerebrospinal fluid is removed or absorbed almost entirely by the blood-vessels of the subarachnoid space, to a very slight degree by the lymphatics, and practically not at all by the ventricles.

The writer believes that the vast majority, if not all, of spina bifidæ are caused by the pressure exerted by an excessive secretion of cerebrospinal fluid, or, what is more probable, some obstruction to its normal outflow. This pressure, acting in early fetal life at different stages of development, prevents the closure at certain points of the bony canal. This theory is applicable to all forms of spina bifida, and has the support of much clinical evidence. This theory should not be confused with the opinion expressed by Förster many years ago, that spina bifida was due to dropsy of the central canal of the cord, which forced out a pro-



trusion through the posterior columns of the cord, causing atrophy of the nerve fibres. Except for syringomyelocoele, which forms only one or two per cent. of all cases, this is now held to be incorrect, as in the great majority of cases the central canal is normal, and in many the nerve fibres are intact.

What are the facts on which rests the theory of intradural pressure? We know that the cord is derived from the epiblast, as is also the skin. These two structures, the cord and skin, remain adherent, until the mesoblastic structures (meninges and bone) insinuate themselves between the cord and skin, which occurs normally in the third month of fetal life.

The vertebræ are developed from four centres of ossification, one for each lamina and one for each half of the body. The laminæ meet in the median line, closing the spinal canal first in the dorsal region, then in the cervical, and last in the lumbosacral regions. The choroid plexuses of the cerebral ventricles are formed by the second month of fetal life, so that the cerebrospinal space contains fluid before the cord and skin are separated by the mesoblast, which should occur in the third month. Therefore, any undue pressure in the spinal canal at this time will prevent the closure at some point of the canal; and it is clear that this point will be the region of latest closure, the lumbosacral region. This is the region favored by spina bifida, in which, according to observations, 86 per cent. of all spina bifida are found; while  $9\frac{1}{2}$  per cent. are found in the cervical, and  $4\frac{1}{2}$  per cent. in the dorsal, the region of earliest closure of the canal.

Even in total rhachischisis with only rudimentary development of the cord and brain, the ventricles and choroid plexuses are fully developed, showing that fluid has been secreted; and excessive secretion with distention at this early stage will account for the rudimentary brain and cord and its open condition.

What are the clinical facts that support the theory of undue subdural fluid pressure, or that oppose the theory of germinal defects or lack of development? As against the theory of lack of development in the mesoblast, we have those cases in which after the protrusion is excised, thus removing pressure, the rudimentary laminæ will take on new growth, as reported by Patterson.<sup>8</sup>

Supporters of the germinal defect theory assert that the increased amount of fluid present, as shown by the hydrocephalus that so commonly accompanies spina bifida, is a secondary condition, a result of the open canal. This is disproved by those cases where there is no bony defect, but the protrusion is forced out through the intervertebral



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ligaments. Also, hydrocephalus does not follow craniotomies or decompression operations, done on very young infants, and yet hydrocephalus will very often develop in children with spina bifida *after* the defect is closed. My own opinion is that the conditions causing the excess of fluid in fetal life still exist after birth, but much of this fluid is removed by the rich vascularization to be seen around the sac, the dura being absent or open in most of these cases. Where the dura is not open, or where hydrocephalus does not follow the operation, is explained by renewed function of the vessels of the subarachnoid space. The series of experiments undertaken by the writer were not done with the expectation of discovering the cause of spina bifida, but rather with the view of discovering evidence for or against the theory of undue intradural pressure. Naturally, it is admitted that producing spina bifida or a condition analogous to it, on a living animal by means of pressure, is not positive proof that spina bifida in the human being is produced by this means, any more than producing spina bifida in frog embryos by treatment with sodium chloride solutions is proof that spina bifida in the human being is caused by chemical stimulation. Experimentation along this line can but add corroborative evidence to clinical facts. Very young dogs were selected and lumbar laminectomies were done, only the superficial tissues being sutured over the defect. Large areas of the skull were removed and wounds allowed to heal. Then pressure was applied to the head, maintained and gradually increased. It was not expected that the external pressure alone would be sufficient to cause a protrusion in the lumbar defect, as even in very young dogs the dura is rather inelastic, but it was hoped that the irritation of the pressure on the cortex would cause an increase in secretion of the cerebrospinal fluid, or, what was equally as efficient, an obstruction to its normal outflow. That this did happen in some of the subjects was shown by the development of œdema of the optic nerve head, which gradually progressed to choked discs with dilated retinal veins, as noted by the ophthalmoscope. This was not due to the external pressure alone, as other dogs, on which as great or greater pressure was used, showed no œdema of the discs. Although the pressure in no case was sufficient to paralyze the dogs, yet in two of them, the one with the choked discs and one other, autopsy showed marked bulging of the spinal membranes through the laminectomy cleft.

The same procedure was carried out on one guinea-pig and two rabbits, with this difference, that injection of salt solution was used to create the pressure, instead of external pressure over a craniotomy wound of the head. Rabbits and guinea-pigs were selected because of

their less strong and dense meninges. The technic was the same in all three cases, and the same results were secured. The laminæ of the last two lumbar and of the first and second sacral vertebræ were removed, exposing the dura. Then the laminæ of the last cervical vertebra was removed and by means of a syringe with hollow needle two drachms of salt solution were injected under the membranes. This increase of intradural pressure caused a marked protrusion of the membranes through the cleft in the lumbosacral region. Fig. 1 shows the artificial spina bifida produced in the lumbosacral region of a rabbit and Fig. 2 is a diagrammatic view of the same condition. Naturally these experiments do not prove the cause of spina bifida. They merely show that intradural pressure, whether applied over a period of weeks, as in the case of the dog, or for a few minutes, as in the case of the rabbit, will cause a protrusion of the spinal membranes if there be a gap or defect in the bony canal. They are evidence, not that spina bifida is caused in this manner, but that it could be. In the writer's opinion, further advances along this line of investigation will be made as more facts are uncovered concerning the disorders to which the cerebrospinal fluid circulation is subject.

VARIETIES OF SPINA BIFIDA.—*Rhachischisis*.—This, the most extreme form, differs from spina bifida proper, in that in it the cord is spread out and exposed and the central canal is open, while in spina bifida proper the cord is covered and the central canal does not open on to the surface. *Rhachischisis* may be either total or partial.

In total *rhachischisis*, the pressure being exerted very early in intra-uterine life, the entire medullary groove remains open, so that the entire canal is uncovered; the skin, bony arches and meninges are absent. The lining of the central canal of the cord is open and the layer of pia containing blood-vessels is exposed. *Anacephalus* sometimes accompanies this condition, so that from the forehead to the coccyx the spinal canal is simply a trough containing the mass of undeveloped brain and cord. The spinal column is usually disposed in abnormal curves, especially in the dorsal and cervical regions. Thorndike,<sup>9</sup> who has studied this condition, presents several typical and interesting specimens of this character.

In partial *rhachischisis* or, as it is termed by some, *myelocoele*, only a part of the spine and cord are involved, usually only three to five vertebræ. At the site of the defect, the cord with its central canal is open, and the spread-out layers of pia carrying blood-vessels gives to this area, which Von Recklinghausen has called the "area medullovasculosa," the appearance of mucous membrane. In milder forms of partial

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rhachischisis the defect is covered by a thin membrane, the central canal opening into the surface at the upper and lower ends of the gap, with leakage of cerebrospinal fluid.

Both total and partial rhachischisis are easily recognized. They are of little interest from an applied surgical point of view, as the infants are usually stillborn, or at best live but a few hours or days. The case of partial rhachischisis with recovery reported by Small<sup>10</sup> is a doubtful one, as nothing was said as to the condition of the cord or that the central canal opened into the surface.

*Myelomeningocele*.—This is the most frequent type of spina bifida, occurring in 70 to 80 per cent. of all cases. In this type of spina bifida the cord is almost fully formed, but the abnormal pressure prevented the crossing over of the mesoblastic tissues, so that the cord and skin are not entirely separated. Hence, when the skin is forced outward to form the sac wall, the adherent cord and roots are drawn out of the canal. Myelomeningocele is commonly found in the lumbar region, infrequently in the dorsal, and rarely in the cervical. Fig. 3 is a myelomeningocele at the lumbosacral junction, accompanied by mild hydrocephalus. At operation eight roots of the cauda equina were found adherent to the sac wall. There is a fairly large bony defect, and these tumors are always sessile. The base of the sac is composed of normal skin, but the apex is covered by a membrane formed by the fusion of epithelium with the arachnoid and pia. This membrane may be quite strong, but is usually thin, and contains small ulcerating areas, through which cerebrospinal fluid "sweats." At the junction of this membrane with the skin base, there is a ring of connective tissue containing plexuses of blood-vessels and at times the rudimentary laminæ. The protrusion is usually unilocular, but occasionally small cavities are found communicating with the main sac. The summit of the sac is often marked by a dimple at the point where the cord is attached, or if the defect is in the lower lumbar region, by a broad furrow marking the attachment of the conus terminalis. Due to the traction of the adherent cord and roots, or to lessened intradural pressure, the entire summit of the protrusion is often cup-shaped. The dura is absent in the defect, extending only to the membranous-skin junction, or even only to the margins of the bone defect. Rarely myelomeningocele is unaccompanied by nerve disturbances, but the following are more often found: Partial paralysis of the legs or complete paraplegia, club-foot, trophic ulcers, incomplete control of the sphincters and often incontinence.

The diagnosis of spina bifida is, as a rule, not difficult, if the following points are kept in mind—that the protrusion is congenital and is in



the median line; that there is fluctuation of the sac, and pressure causes a decrease in size with bulging of the fontanelle; that the tumor becomes tense on coughing or crying; that the cleft in the bone may be felt; that the tumor is translucent.

Spina bifida in the lumbosacral region must be differentiated from the following conditions: Lipoma, post-rectal dermoid, and ischiatic hernia. The most common error is made in regard to lipoma. Lipoma often overlies a small spina bifida and operation to remove a supposedly simple lipoma may result disastrously for the patient (Bland Sutton<sup>11</sup>).

To differentiate between the different varieties of spina bifida is more difficult. In making a diagnosis of myelomeningocele we rely upon the following points: Myelomeningocele is the most common form, occurring in 70 to 80 per cent.; there is usually a fairly large bony cleft which can be felt; the tumor is sessile and has a membranous apex, which is dimpled or furrowed at the point of attachment of the cord or roots; transillumination will usually show the extruded cord and roots, but this sign often fails, owing to irregularities in the sac wall; and, finally, the evidence of nerve involvement of the lower extremities, which is very common in myelomeningocele.

Untreated, practically all these children will die, very few of them reaching the age of five years. Operated upon, the prognosis depends upon the general condition of the child, the condition of the sac and the amount of nerve involvement. There have been many cases of cure reported, most of them in young infants.

*Spinal Meningocele.*—Meningocele is found in from eight to twelve per cent. of all cases. It is commonly found in the lumbosacral region, infrequently in the cervical and rarely in the dorsal regions. The bony gap is usually a small one, involving but one or two arches. Occasionally there is no bony defect found, the meninges being forced out through the intervertebral ligaments. The protrusion is at times pedunculated and covered with normal skin (Fig. 4), though sometimes the apex contains a small membranous area. The inner sac wall is lined entirely with dura and contains only fluid, the cord and nerve roots not lying in the sac, but occupying their normal positions in the canal.

Meningocele, the simplest form of spina bifida, can be explained in this manner: The abnormal accumulation of fluid does not occur until some time in the third month of fetal life, after the separation of cord and skin by the mesoblastic tissues. The pressure finds its outlet at the point where solid closure is least advanced, the lumbosacral region. When the protrusion has a very slender pedicle, the opening into the canal may be obliterated by fibrous tissue.

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The diagnosis of spinal meningocele rests on the following: The sac has a fairly narrow base, but rarely pedunculated. It is usually covered entirely by normal skin. Transillumination shows the absence of nerve elements. Nerve supply of the lower extremities is entirely, or almost entirely, free from involvement.

The prognosis is good, if operation is performed, though frequently excision of the sac is followed by enlargement of the head. Untreated, the prognosis is bad, for, except in those few cases where the opening into the canal is occluded, the tumor increases in size, with rupture and septic meningitis as the result.

*Syringomyelocoele.*—This very rare form of spina bifida is due to the pressure exerted by an abnormal amount of cerebrospinal fluid in the central canal of the cord, the pressure preventing the closure of the bony arches and forcing the posterior half of the cord out through the bony defect. Thus the inner sac wall is formed from the spread-out cord, with attenuation and atrophy of the nerve elements. Syringomyelocoele is found usually in the lumbar region, rarely in the cervical. As the central canal of the cord in the lumbar region remains quite large almost until birth, a collection of fluid here with pressure readily accounts for the protrusion being found in this region.

In making a differential diagnosis of syringomyelocoele from the other forms of spina bifida, its rarity must be taken into account. It occurs only in one to two per cent. of all cases. In translucency it resembles meningocele, as the attenuated nerve elements cast little shadow. In appearance and symptoms of nerve involvement, it closely resembles myelomeningocoele. However, as operation is the treatment for both types, a positive diagnosis before the sac is opened is not of great importance. The prognosis of syringomyelocoele if untreated is the same as for myelomeningocoele, and with operation it is not as favorable as that for myelomeningocoele.

*Anterior Spina Bifida.*—In this rare form, the protrusion extends forward between the two halves of the bodies of the vertebræ, which, as has been said, develop from two centres of ossification; or through an intervertebral foramen. In this type the sac is usually found in the abdomen or pelvis, and the sacrum is the part of the spinal column most often involved. As a rule, there is no posterior deformity of the arches, though Williard<sup>12</sup> reports a case in which there was both an anterior and posterior protrusion. Spina bifida anterior is almost entirely confined to females, though Grossman reports one in a male infant of ten months. It is a pure meningocele, though pressure or irritation may cause some nerve disturbances, usually of the motor nerves.



The diagnosis is exceedingly difficult unless there is also a posterior protrusion, or there is an accompanying nerve involvement, such as club-foot or paraparesis. The sac usually reaches a much greater size than could occur posteriorly without rupture, and it is usually mistaken for sarcoma or ovarian cyst. The presence of symptoms of nerve involvement of the lower extremities should prevent such errors. The prognosis is uniformly bad, as all cases operated upon reported to date have died. In the majority of cases it would have been most difficult to have successfully closed the opening into the spinal canal.

*Spina Bifida Occulta.*—In this curious and interesting form of spina bifida there is a cleft in the bony arches, but no protrusion. The absence of protrusion is accounted for by lessened intradural pressure or by rupture of the sac in early fetal life, the point of rupture being marked by a scar which is often found in the skin over the defect. The tissues over the defect are often the seat of a diffuse non-capsulated lipomatous growth, or the skin overlying it is wrinkled and pigmented and surmounted by a tuft of coarse hair. The presence of lipoma or of hypertrichosis is equally pathognomonic of spina bifida occulta. Occasionally, however, the overlying tissues are free of defects and the skin is normal and free of scars or hair. Very often a lipoma or dermoid lies in the bony cleft or in the spinal canal, connected by fibrous bands with another tumor outside the canal. Again, adhesions are often found connecting the skin and cord and roots, showing an imperfect separation of the two in fetal life. Nerve involvement is usually absent at birth, but with the growth of the child, the ascent of the cord drags upon the adhesions in the cleft, and more or less severe symptoms of nerve disturbances make their appearance in the lower extremities. These are, weakness of the legs, distortion of the feet, coldness and discoloration of legs, trophic ulcers and disturbances of the sphincters.

The diagnosis depends on the symptoms of nerve involvement, presence of lipomatous tissue or hypertrichosis over the lower spine, and on the X-ray.

The patient in Fig. 5 was a sturdy sailor twenty-four years of age, who complained only of tingling in the hands and fingers when the arms were hanging loosely. There were areas of hypæsthesia and hypalgesia on outer side of the left upper arm. The skin over the defect was normal; no hypertrichosis or lipoma was present. The X-ray (Fig. 6) showed a defect extending from the fifth cervical to the sixth dorsal vertebra (the arrows mark the upper and lower limits of the defect). There will be noticed in this picture and also in the other skiagraphs a spreading or broadening of all parts of the defective vertebræ, which I

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ascribe to the effects of the intradural pressure in the developmental stage. Dr. B. C. Darling, who has made a study of this condition from a skiagrapher's point of view, tells me he finds this "broadening" in all cases.

The child of four and a half years shown in Fig. 7 had spina bifida occulta in the lumbosacral region, with partial paraplegia and incontinence of urine from birth. No protrusion in back or hypertrichosis was present, but a diffuse lipoma over the sacral region. The X-rays (Fig. 8) show absence of the laminæ of the fifth lumbar vertebra and the upper segments of the sacrum, with distortion of the sacrum and the pelvis. Fig. 9 is the skiagraph of the pelvis of a girl of nine years of age who had partial paralysis of the right leg with a congenital dislocation of the right hip and a dilated bladder with incontinence. There was a tuft of hair an inch long over the fifth lumbar vertebra, but no protrusion. Fig. 10 shows the defect in the laminæ better, extending from the fifth lumbar vertebra to the fourth sacral segment, a case of spina bifida occulta.

It was formerly believed that congenital dislocation of the hip, club-foot, hare-lip, cleft palate and the other deformities that sometimes accompany spina bifida, were due to general lack of development, and proving that spina bifida was but a germinal defect. But club-foot and dislocation of the hip, as in the above case, are readily seen to be due to the defective nerve supply. They are consequences of spina bifida and not germinal defects. As for hare-lip and cleft palate, we know that cyclopia and non-union of the branchial clefts can be artificially produced in the lower vertebrates by interfering with their normal course of development, by chemical agents. And as the normal union of the frontonasal and maxillary processes depends on a normal development of the forebrain region, the pressure of an abnormal accumulation of cerebrospinal fluid in fetal life will account for these defects.

**TREATMENT.**—The treatment of spina bifida other than by operative interference may be dismissed in a few words. Ligation of the base of the sac, acupuncture and aspiration only hasten the rupture of the sac, and are no longer used. Injection of the protrusion with Morton's fluid, a solution of iodine, once widely used, usually results in death. Even if shrinkage of the sac followed the injection, if any nerve elements were present in the sac, further compression of these occurred. However, some surgeons still advocate the use of Morton's fluid. Open operation is coming more and more to be recognized as the rational and best method of treatment. By many surgeons operation is strictly lim-

ited to selected and favorable cases, without much nerve involvement. But in view of the fact that over 90 per cent. of these children will die in the first year alone, if not relieved, and that many cases of recovery following operation on apparently hopeless cases have been reported, the scope of operative interference should be greatly extended. The writer believes that the only contra-indications to operation are a bony defect so large that it could not possibly be repaired, and a condition of absolute paraplegia and complete loss of sphincteric control. Age is of no importance, as many cases of recovery are reported in very young infants, following operation.

A description of the operative technic and the after-treatment will be omitted here, as the writer has described them in detail elsewhere (Johnson's *Operative Therapeutics*, vol. iii). The following series of cases, which were operated upon in conjunction with Dr. William Sharpe, in the Neurological Surgical Department of the N. Y. Polyclinic Hospital, were selected for reporting as representing different types of spina bifida. They include myelomeningocele, meningocele and spina bifida occulta. I have not yet met with syringomyelocele nor spina bifida anterior.

It is interesting to note that in the majority of them there was an associated hydrocephalus.

CASE I.—*Spinal Meningocele with Hydrocephalus*.—P. M., age three months; full-term child; normal delivery. At birth large head noticeable, also lump on back size of English walnut, which at times became much smaller, leaving only a wrinkled pad of skin. Examination at three months showed head quite large and broad, with bulging forehead, and fontanelles tense. There was a protrusion the size of a small grape-fruit over the sacral region two inches from the anus. Definite weakness of the legs. Child rather stuporous, some difficulty in breathing.

*Operation*.—Thin-walled meningocele, no cord elements in sac. Inner sac wall sutured at margins of cleft, and fascia drawn over and sutured with three layers of chromic gut. Skin sutures of silk. Right ventricle was tapped through a small opening and four strands of No. 2 catgut were passed into ventricle and anchored under scalp for drainage. At conclusion of operation child was in fair condition. Temperature rose to  $107^{\circ}$  in twelve hours and child died. In this case, we probably attempted to do too much, but on account of the difficulty in respiration, we thought it unwise to defer the tapping of the ventricle to a later time.

CASE II.—*Myelomeningocele with Hydrocephalus*.—Baby N., age five months; first baby; full term; normal delivery. Small





FIG. 1.—Artificial spina bifida in rabbit.

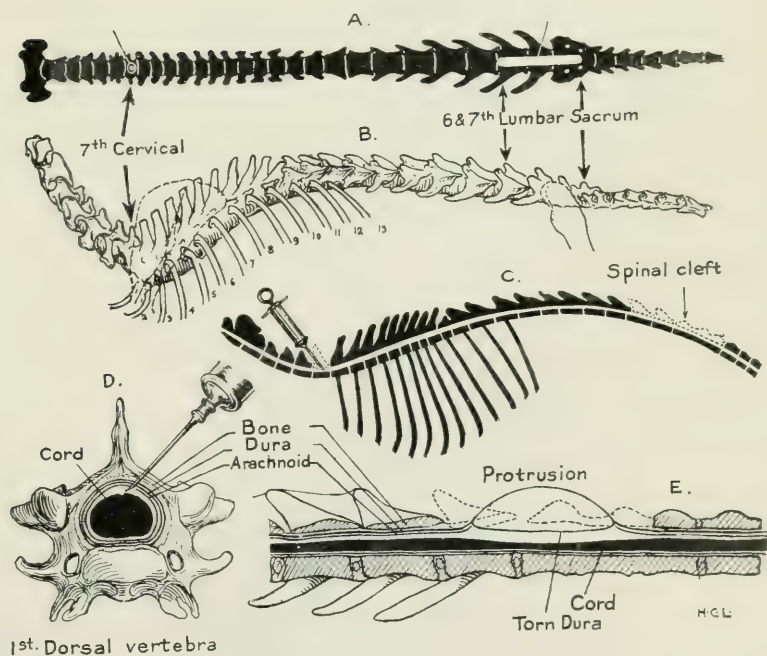


FIG. 2.—Diagrammatic scheme of artificial spina bifida.



FIG. 3.—Case II. Myelomeningocele with mild hydrocephalus.



FIG. 4.—Case III. Spinal meningocele with hydrocephalus.



FIG. 5.—Spina bifida occulta in cervicodorsal region.





FIG. 6.—Skiagraph of Fig. 5 (skiagraph by Dr. B. C. Darling).



FIG. 7.—Spina bifida occulta in lumbosacral region (after operation). A, line of incision.



FIG. 8.—Skiagraph of Fig. 7 (skiagraph by Dr. B. C. Darling).



FIG. 9.—Spina bifida occulta in lumbosacral region, with congenital dislocation of right hip. (Permission of Dr. Royal Whitman, skiagraph by Dr. B. C. Darling.)

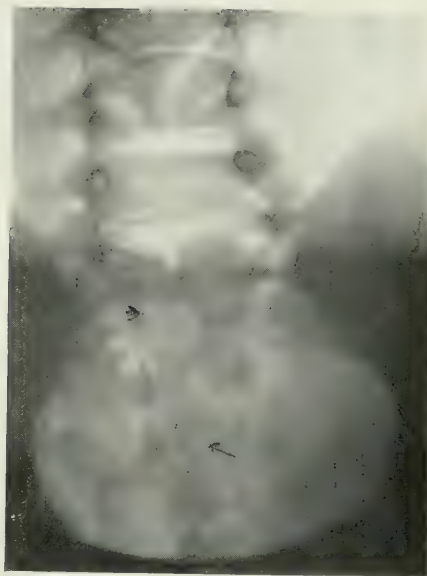


FIG. 10.—Another view of sacrum in Fig. 9.



FIG. 11.—Case II. Myelomeningocele with hydrocephalus (after operation). Fig. 3 is same case before operation.



FIG. 12.—Case IV. Myelomeningocele (after operation).



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lump noticed at birth in lower lumbar region. This gradually increased in size. Legs apparently not affected. Examination at five months showed a well-nourished child with somewhat weak legs, but no definite paralysis. Slight weakness of rectal sphincter. In the lumbosacral region there was a reddish, thin-walled cystic tumor the size of a grape-fruit, with a wide base, three inches in diameter. Sac wall very thin at several points, rupture appearing imminent. Head was mildly hydrocephalic with high towering forehead (Fig. 3).

*Operation.*—A curvilinear incision was made along the left base of the sac. The lowered head of the child prevented the escape of cerebrospinal fluid other than that contained in the sac. Bone defect small,  $2\frac{1}{2}$  cm. in length. Eight roots of the cauda equina were found adherent to the sac wall. These were dissected free and returned to the canal which at this point was very shallow. The dura extending only to the bone margin, the canal was perforce left open. The vertebral aponeurosis was dissected up on each side and sutured over the cleft with several rows of chromic gut; skin sutures of silk. A rubber tissue drain was inserted. Child in good condition after operation.

Several days after operation several small trophic ulcers appeared on inner sides of thighs and on left big toe, probably due to operative injury to nerves in sac wall. They healed in a short time. At present, one year after operation, child is in good condition, the legs are strong and there has been no further enlargement of the head (Fig. 11).

CASE III.—*Meningocele with Mild Hydrocephalus.*—J. M., age four months; full-term child; instrumental delivery. Congenital protrusion the size of a lemon in lumbosacral region. No paralysis of lower extremities. Head apparently normal. Examination at four months showed a fairly well-nourished child with a thick, reddened tumor, orange-sized, over the fourth and fifth lumbar vertebræ. Tumor cystic in places. No paralyses, no sphincteric disturbances. Head slightly enlarged, but scalp vessels were greatly dilated and fontanelles tense (see Fig. 4).

*Operation.*—Straight incision in median line. Cord and nerve roots not involved in sac. Small laminal defect, through which a small cyst of arachnoid protruded (sac within sac). Base of sac ligated and overlaid by flaps from surrounding fasciæ, which was sutured with chromic gut; skin sutures of silk. Right ventricle tapped through the right margin of the anterior fontanelle. Much fluid escaped. Two weeks later the head had slightly enlarged, with fontanelles tense. Right ventricle was again tapped and ten days later this tapping was repeated. At present writing the child is in good condition. The head is still large, but not enlarging.



CASE IV.—*Myelomeningocele with Mild Hydrocephalus*.—A. H., age two weeks; full-term; normal delivery. Congenital cherry-sized swelling in lumbosacral region. Did not move the legs freely. Head not enlarged. Examination showed a well-nourished child with a reddened, tense swelling, orange-sized, over the first sacral vertebra. Sac wall very thin, with two yellowish excoriations at the summit. Head not much enlarged, but fontanelles very tense. Some weakness of right leg. Incontinence of urine and fæces.

*Operation*.—S-shaped incision opening sac. A number of cauda roots were found adherent to sac wall, dissected free and returned to the canal. Small bony defect in the first sacral segment. Inner sac wall sutured in the cleft and overlaid by flaps cut from the vertebral aponeurosis which were drawn one under the other, as in the repair of umbilical hernia. Skin sutures of silk. Superficial infection of wound from the dribbling urine and fæces. Daily dressings. Child discharged three weeks later in good condition. Five months later there was no paralysis, no incontinence; head slightly enlarged. A year later child was in excellent condition, no paralysis and head not enlarged (see Fig. 12).

CASE V.—*Myelomeningocele with Almost Complete Paraplegia*.—G. M., age one and a half years; eight-months child; normal delivery. Tumor in lumbosacral region size of walnut which ruptured at birth and discharged fluid for three days. Legs weak. Tumor gradually increased to orange size and was treated by caustics which caused it to shrink somewhat, with intense induration. Legs gradually became almost completely paralyzed, with incontinence of urine and fæces. Examination showed a fairly well-nourished child with paralysis of both legs and loss of sphincteric control of bladder and rectum. In the lumbosacral region was a reddened indurated mass the size of an orange. In the centre was a thinned area one and a half inches in diameter. No hydrocephalus.

*Operation*.—Straight vertical incision through centre of mass. Many nerve roots found bound in the scar tissue. Bony defect in the laminæ of the three lower lumbar vertebrae two and one-half inches long. Nerve roots were dissected free with much difficulty and delay and replaced in canal, and the tissues containing the rudimentary laminæ drawn together with chromic gut. Flaps from the lumbar muscles were resected and drawn over the cleft and sutured, with double row of gut. Skin with silk. Child apparently in fair condition but died in a short time after removal to the ward.

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The results obtained by the application of caustics to the sac (increase of paralysis) are identical with those following injection of the sac with irritants (Morton's fluid) if the protrusion contains nerve elements.

CASE VI.—*Spina Bifida Occulta with Paralysis of Legs*.—B. S., age four and one-half years; full-term child; normal delivery. Paralysis of legs not complete, from birth, and urinary incontinence. No rectal disturbance. Right leg more paretic than left. Examination showed at the lumbosacral juncture a diffuse lipomatous growth which extended over the left buttock (see Fig. 7). The prominence of the left buttock is due to the lipoma which extended over the cleft. No hypertrichosis. No defect could be felt in the spine, but the X-rays showed a defect in the fifth lumbar vertebra and the two upper segments of the sacrum, extending more to the left side (see Fig. 8). Legs markedly paretic, with marked atrophy. Knee-jerks absent. No Babinski. Sensation normal. Incontinence of urine.

*Operation*.—S-shaped incision (Fig. 7) over the defect as noted by the X-rays. Mass of fat overlying the defect and found in the cleft. Dura absent in the gap. Many adhesions found among the roots of the cauda, but no protrusion through the cleft. The adhesions found were removed and also the mass of tissue lying in the cleft. Lumbar fascia drawn over the cleft and sutured by double row of chromic gut. Skin with silk. Dressed daily. No infection. Three months later there was no improvement in paralysis or incontinence. Legs were somewhat larger and right knee-jerk was obtainable. Her present condition is about the same. In this case, contrary to that of Case I, we probably did not do enough, and a second operation is contemplated.

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- <sup>12</sup> Williard, de F.: ANN. SURG., 1904, xxxix, 612.



# Hibbs' Osteoplastic Operation for Pott's Disease

A Report of Clinical Observations with Results in One Hundred and Fifty-Eight Cases, and Interpretation of  
Experimental Studies in Animals

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NEW YORK





# HIBBS' OSTEOPLASTIC OPERATION FOR POTT'S DISEASE\*

A REPORT OF CLINICAL OBSERVATIONS WITH RESULTS  
IN ONE HUNDRED AND FIFTY-EIGHT CASES,  
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About half a century ago Taylor and Sayre demonstrated the principles of mechanical support in the treatment of Pott's disease. Since that time the routine has been to apply, in the case of ambulatory patients, either a Taylor spinal assistant, or a plaster-of-Paris jacket. More recently a Bradford or Whitman frame has been employed whenever the recumbent position was indicated. While these forms of treatment have resulted in a large percentage of cures, they have confessedly left much to be desired. Even the best apparatus is cumbersome and needs constant supervision; and in most cases only imperfect results can be obtained even after years of tedious treatment. In no branch of surgery, perhaps, is the social status of the patient in such close relationship to the possibility of cure. Among the well-to-do tuberculous lesions in the cervical and lumbar regions can be dealt with in a fairly satisfactory manner. The repair, however, of similar lesions in the dorsal region is usually a failure anatomically, although functionally good, because of the impossibility of immobilization. If such is the case under satisfactory social conditions, how much more unfavorable is the outlook for the poor

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\* Read before the Section on Orthopedic Surgery at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

\* From the New York Orthopedic Dispensary and Hospital, and from the Laboratory of Physiological Surgery, New York University.



Fig. 1.—The spines and the posterior aspect of the vertebrae are stripped of periosteum, which is shown in circular white areas. The spines have not as yet been cut and imbricated.



Fig. 2.—Dog 167, sixty-eight days: non-union owing to deficient time.

dispensary patient! General recognition of these facts has led a number of men to attempt operative treatment of Pott's disease.

Prior to 1908 no definite results were obtained, but in that year F. Lange implanted two tin-plated wire splints with bulbous ends beneath the muscles over the diseased area. These lay on either side of the spinous processes, their ends being attached to them by a silk suture. Two years later<sup>1</sup> the symptoms had subsided, deformity had not increased, and the splints had remained in place.

It has long been known from studies on the healed kyphos that in many instances a fusion of the posterior aspect of the vertebrae through the laminae and spinous processes is the method by which Nature effects repair. Herein, obviously, is the key to the situation. If the surgeon could in a few weeks cause the fusion which it took Nature months or years to bring about, he could not well fail to stay the course of the disease and limit the deformity. Thus considered, the question became simply one of determining the best technic for causing arthrodesis of the lateral articulations and bridging the intervertebral spaces, thereby fusing the entire dorsal aspect of the vertebrae. Early in the year 1910 it became my privilege to assist Dr. R. A. Hibbs in his studies on the cadaver which led him to devise the technic which experience has shown to be both anatomically satisfactory and surgically acceptable. While it was easily demonstrable that in adult and adolescent life there was always adequate bone *in situ* to make the bridge, it was necessary in the case of very young children to await a verdict which should be based on actual findings at the operating table. It is gratifying to report that adequate bone exists at *all* ages; therefore the use of the autoplasmic bone transplant, or any other form of foreign body, is not necessary. The use of such bone transplants had at first been deemed necessary in the case of younger children, but operative experience has demonstrated their uselessness.

The first account of Hibbs' operation<sup>2</sup> was published in 1911. He also described his method in a

1. Lange, F.: Jour. Am. Orthop. Assn., November, 1910.

2. Hibbs, R. A.: New York Med. Jour., May 27, 1911.

paper<sup>3</sup> read before the Section on Surgery of the American Medical Association, at Atlantic City, June, 1912. From this latter paper is taken the author's account of his operation, as follows:



Fig. 3.—Dog 167, sixty-eight days: non-union owing to deficient time.

In performing the operation, a longitudinal incision is made directly over the spinous processes, through skin, supraspinous ligament and periosteum, to the tips of the spinous processes. The periosteum is split over both the

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3. Hibbs, R. A.: An Operation for Pott's Disease of the Spine, *THE JOURNAL A. M. A.*, Aug. 10, 1912, p. 433.



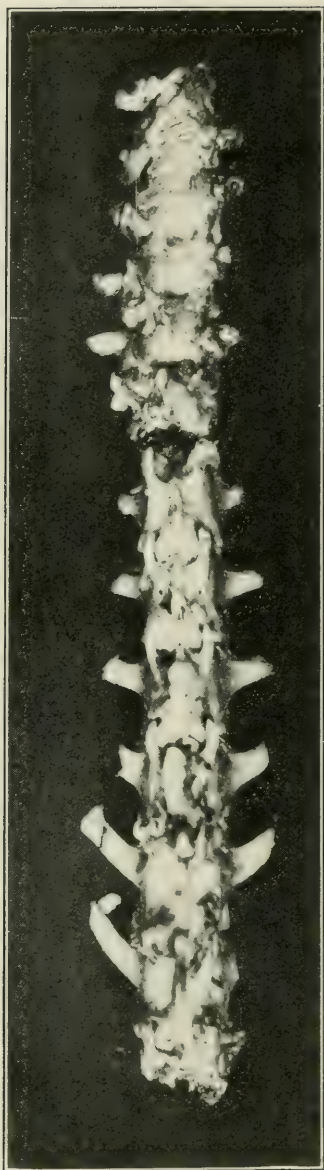


Fig. 4.—Dog 187, sixty-two days: non-union owing to deficient time. Accidental fracture of spine in preparation of specimen.

upper and lower borders of the spinous processes and the laminae, and stripped back from them to the base of the transverse processes. The spinous processes are then transposed after partial fracture, so that they make contact with fresh bone, the base of each with its own base and the tips with the base of the next below. The adjacent edges of the laminae being absolutely free from periosteum, a small piece of bone is elevated from the edge of the laminae and placed across the space between them, its free end in contact with the bare bone of the laminae next below it.

The lateral walls of periosteum and the split supraspinous ligament are brought together over these processes by interrupted chromic catgut sutures. The skin wound is closed by silk, and a steel brace applied. Detailed operative and postoperative directions follow.

The only addition to this technic has been as follows: The lateral articulations are exposed and the cartilage removed by a very small curet. This adds to the extent of the fusion.

We have now had ample opportunity to test the value of this operation. It would be too much of a tax on your time and patience to detail the nearly two hundred cases which have been treated by this method in the New York Orthopedic Hospital; therefore, I will briefly summarize the main features in the cases so treated during the years 1911, 1912 and 1913.

*Summary 1911.*—There were twenty-two cases, ranging in age from 5 years to 25 years; the duration of the disease was from two months to thirteen years; six had formerly worn plaster jackets; sixteen had worn spinal assistants; the range of the deformity was from three to twelve vertebrae; in six cases psoas spasm was observed, psoas abscess in two, and increased reflexes in eight; the number of vertebrae fused varied from five to fourteen.

*Summary 1912.*—There were seventy-two cases, ranging in age from 3 to 41 years; the duration of the disease was from four weeks to twelve years; six had formerly worn plaster jackets, thirty-seven spinal assistants and one Bradford frame; the range of the deformity was from three to twelve vertebrae; fifteen showed exaggerated reflexes, eight, psoas abscess and nineteen psoas spasm; the extent of the operation varied from five to fourteen vertebrae.

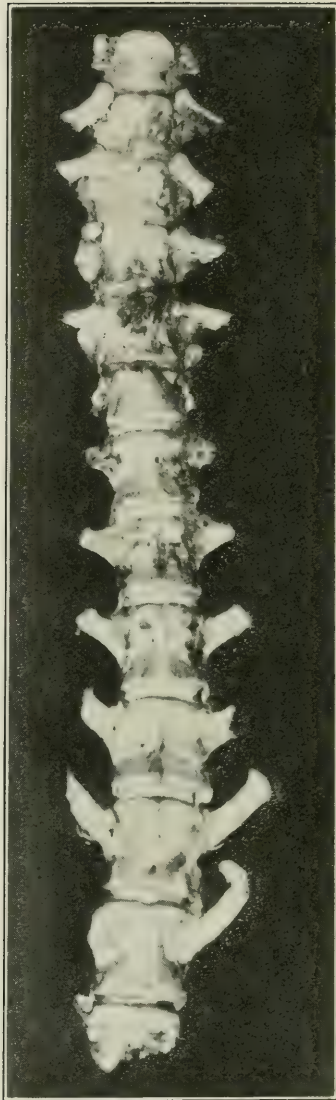


Fig. 5.—Dog 187, sixty-two days: non-union owing to deficient time. Accidental fracture of spine in preparation of specimen.

*Summary 1913.*—There were sixty-four cases, ranging in age from 18 months to 14 years; forty had previously worn spinal assistants, two had undergone bone transplantation from the tibia, and four had previous osteoplastic operations, an insufficient number of vertebrae having been included; the range of the



Fig. 6.—Result on normal dog's spine of osteoplastic technic (Hibbs').

deformity was from six to fourteen vertebrae; in twenty-three cases psoas spasm was observed, psoas abscess in two and increased reflexes in seventeen; the extent of the operation varied from eight to fourteen vertebrae.

Of the 158 patients seven have died, and four required reoperation for the above-mentioned reasons. With these exceptions, the results have been eminently satisfactory, inasmuch as, barring three who were paralyzed when they came to the hospital, all the symptoms of Pott's disease other than the deformity have disappeared; all the patients who have been operated on for a longer period than one year are without apparatus, and are able to carry on the ordinary avocations of life, whether play or business.

Of the seven who died, it should be noted that the cause of death was in every case extrinsic, and not due to the operation. One died one and a half years after the operation; cause of death, miliary tuberculosis; one died six and a half months after the operation, cause of death, tuberculous meningitis; one died sixteen months after operation, cause of death tuberculous meningitis; one died one and a half years after operation, cause of death, miliary tuberculosis; one died a year and ten months after operation, cause of death, tuberculous meningitis; one died three months after operation, cause of death, pyemia, the patient having been infected before he entered the hospital; one died a year after the operation, cause of death miliary tuberculosis.

Necropsy on two of these cases showed, so far as the field of operation was concerned, a complete fusion of laminae and spinous processes from the lateral articulation on one side to the lateral articulation on the other side, the fusing bone mass in both instances being thick, strong and efficient, thereby proving that the operation itself had been perfectly successful.

In the four cases referred to in which reoperation was required, because an insufficient number of vertebrae had been included in the original operation, an incision was made through the old scar, the original field of operation was exposed, and the vertebral fusion present was found complete, but too short. After healthy vertebrae were included both above and below, the results were as satisfactory as in the other cases. The bone production is easily demonstrated by Roentgen ray in most cases, but the chief value of the roentgenograms is as a preoperative guide to indicate the number of vertebrae which should be fused.



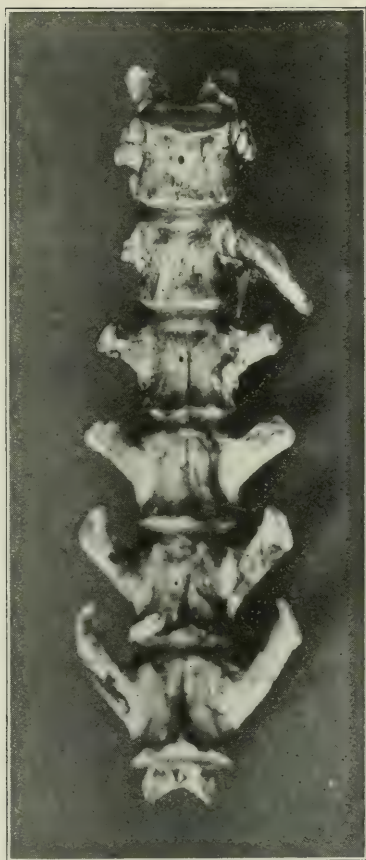


Fig. 7.—Result on normal dog's spine of osteoplastic technic (Hibbs').

The experimental series may be classified as follows :

Dog No.	Date of Operation	Date and Cause of Death	Days Old
172	March 23	March 27, meningitis	4
178	March 25	March 27, shock?	2
177	March 24	March 31, meningitis	7
126	March 22	March 25, shock?	3
127	March 22	March 28, meningitis	6
188	April 1	April 10, meningitis	9
189	April 1	Still living	
175	March 24	March 27, nephritis	3
104	February 5	Still living	
167	March 20	Still living	
166	March 20	Still living	

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**A PRELIMINARY REPORT ON A STUDY OF THE PROTECTIVE FERMENTS OF THE BLOOD BY THE ABDERHaldEN METHOD, AFTER THE TRANSPLANTATION OF ORGANS \***

BY CHARLES GOODMAN, M.D.  
OF NEW YORK

At the recent meeting of the International Congress of Surgeons, Carrel reiterated his former statements to the effect that he had met with considerable success in autotransplantation but that homotransplantation of an organ, such as the kidney, was only temporarily successful, it invariably showing degenerative changes within a few days. Lexer, on the other hand, showed that he had succeeded in overcoming some of the biochemical reactions between his animals by a prolonged preliminary treatment of the host with tissues and blood serum taken from the donor.

Blood-vessels transplanted with proper precautions retain their vitality, become an integral part of the system and are believed to remain without extensive tissue metamorphosis.

But when parenchymatous organs with a more complicated physiological function, such as the kidney, the spleen and the thyroid, are transplanted the results as stated are different. They soon undergo autolytic changes and eventually become absorbed. This is known to be caused by biochemical reactions but may be due in part to injury incident to deficient venous drainage, and the technic about to be described is thought to minimize such injuries.

For an interval after an organ is transplanted, it remains in a state of vasomotor paralysis, and is apt to become overdistended with blood on account of insufficient venous drainage. Before appreciating the value of and employing end-to-end anastomosis I had found it necessary to split the kidney capsule in order to prevent parenchymatous destruction by hypertension.

In transplanting the kidney of one dog to the neck of another, one may unite the renal artery end to side to the carotid, but the stoma of the renal vein (Figs. 1, 2 and 3) should be placed end-to-end with that of the external jugular. This I consider very important, because it creates immediate venous drainage for the transplant on account of the

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\* From the Laboratory of Experimental Surgery, New York University.

negative pressure in the jugular. Such positive drainage does not occur if the anastomosis is lateral.

The Abderhalden method was used to seek the protective ferments in the blood which are brought into activity by the presence of a foreign transplant and which may induce its final autolysis.

The thyroid, on account of its accessibility and of the ease with which slight degenerative changes may be recognized, was chosen as the organ to transplant in this study. Furthermore, its venous drainage may be made adequate to prevent hypertension, thus minimizing parenchymatous changes due to physical injury (Fig. 4).

Thyroid transplantation had been undertaken by Borst and Enderlein, Stich and others. Stich in his series of experiments had two successful autotransplants. Of my autotransplants, in two consecutive instances, the thyroid having been removed from the body and reimplanted in the same animal, the results were satisfactory, the thyroid tissue retaining its normal appearance and, apparently, its activity (Figs. 5, 6 and 7).

In a series of homotransplants, although several of the animals lived for some time, the transplant invariably underwent degenerative changes with absorption (Figs. 8 and 9). From a series of fourteen specimens so far obtained at the Laboratory of Experimental Surgery at the New York University, work conducted through the courtesy of Dr. George D. Stewart, it has been possible in eight instances to demonstrate the presence in the blood of a protective ferment capable of digesting suprarenal tissue. The significance of the demonstration is problematical but it may be an index of the susceptibility of the suprarenal body to insults occurring anywhere in the hæmopoietic system. However this may be, the Abderhalden reaction was positive in eight specimens from dogs operated upon as above described.

Tests with different substrata are being made to determine whether organs other than the suprarenal are sensitive to a thyroid transplant.

It is hoped that a way may be found, perhaps with the aid of the X-ray in controlling lymphatic absorption, to modify the biochemical differences which at present cause autolysis and prevent the use of transplants in applied surgery.

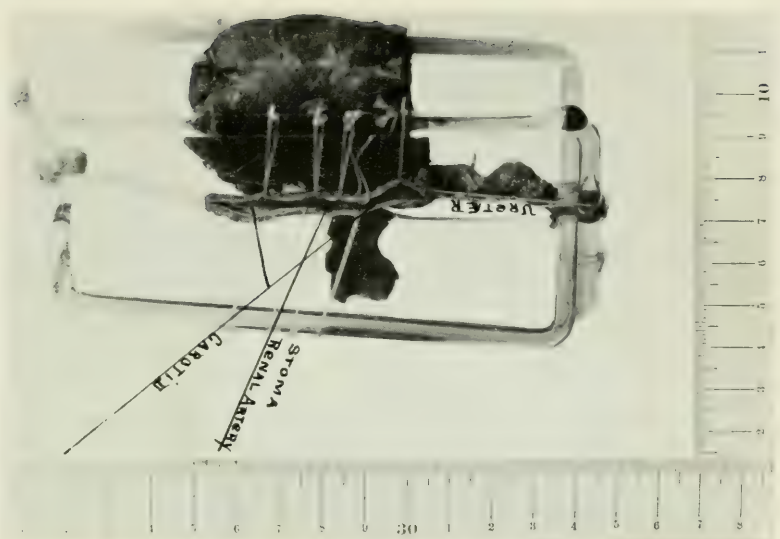


FIG. 1.—1c. Homotransplant of kidney.



FIG. 2.—1b. Homotransplant of kidney.



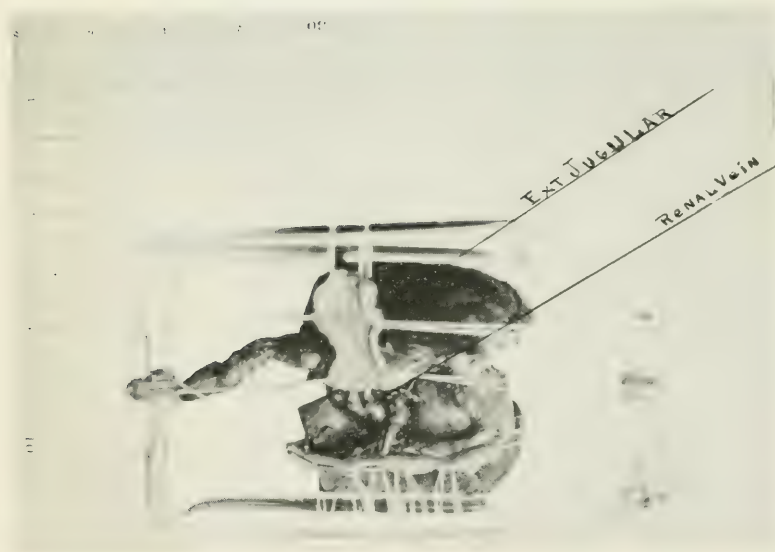


FIG. 3.—1a. Dog 765, host. Dog 685, donor. Homotransplantation of kidney to neck. Terminal anastomosis, left renal to right carotid; end to end renal to external jugular. Removed 8 days post-operative. Note difference in calibre of vessels.

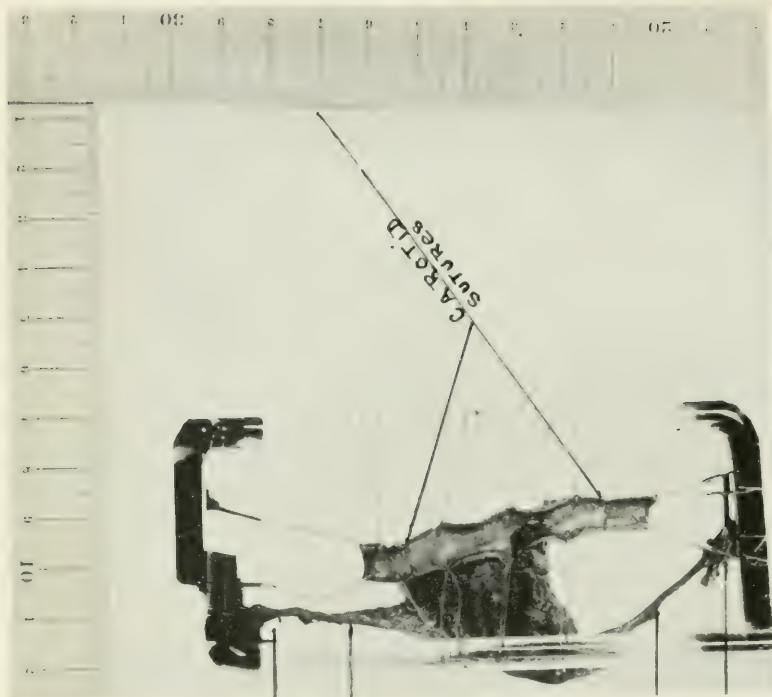


FIG. 4.—Dog 185, moribund black medium sized mongrel, donor. Dog 208, Irish terrier, brown mongrel, host. Homotransplant of thyroid, April 9, 1914. Segment of left carotid of dog 185 interposed between severed ends of right carotid of dog 208. Inferior thyroid vein end to end with left external jugular; superior thyroid vein end to end with right internal jugular. Dog died fifth day, hemorrhage.

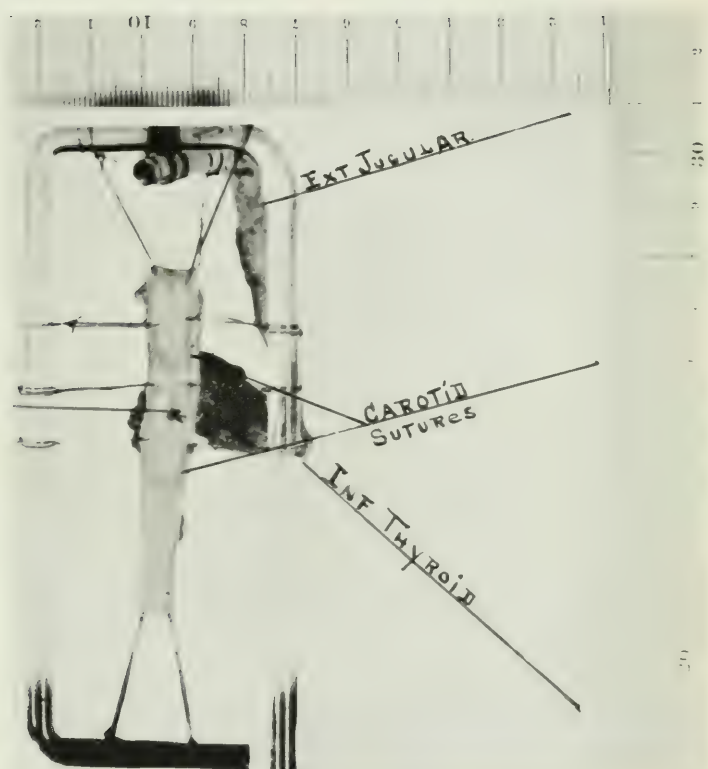


FIG. 5.—Dog 132. Autotransplantation of thyroid, February 26, 1914. Right thyroid with segment of carotid transplanted to left side. Inferior thyroid vein end to end with right external jugular. Removed twenty-three days after operation. Pathological report, normal gland.

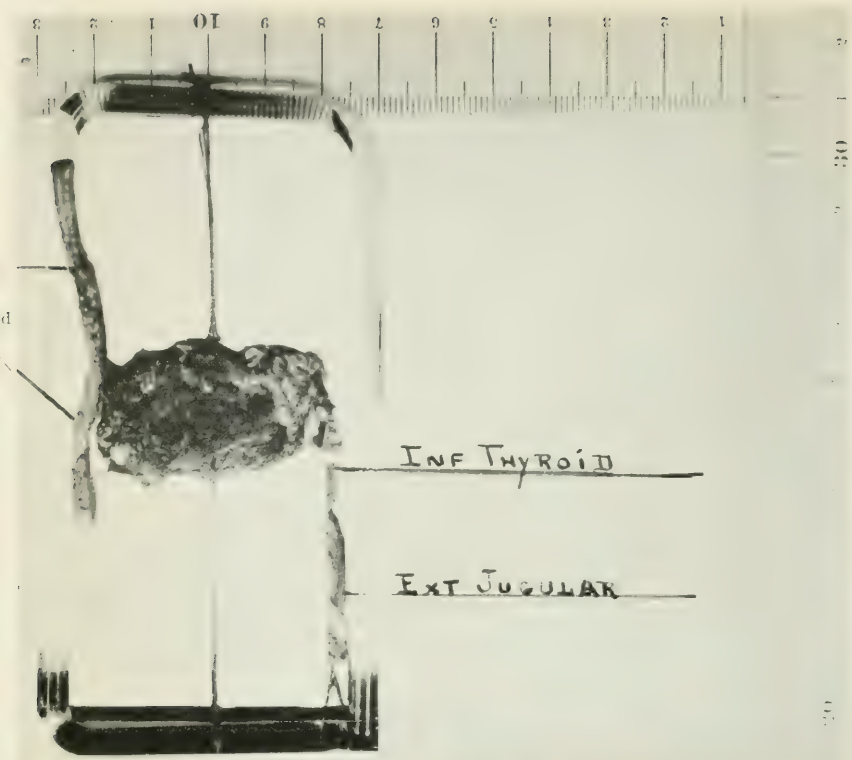


FIG. 6—Dog 138. Autotransplant thyroid, March 2, 1914. Thyroid with segment of right carotid interposed between ends of severed left carotid; right inferior thyroid vein end to end with external jugular. Death due to pericardial hemorrhage, following aspiration of the left ventricle.

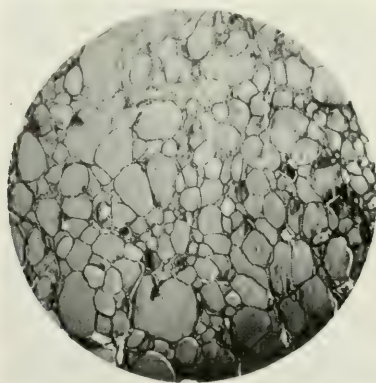


FIG. 7—Dog 132. Autotransplantation of thyroid; specimen removed twenty-three days after operation.

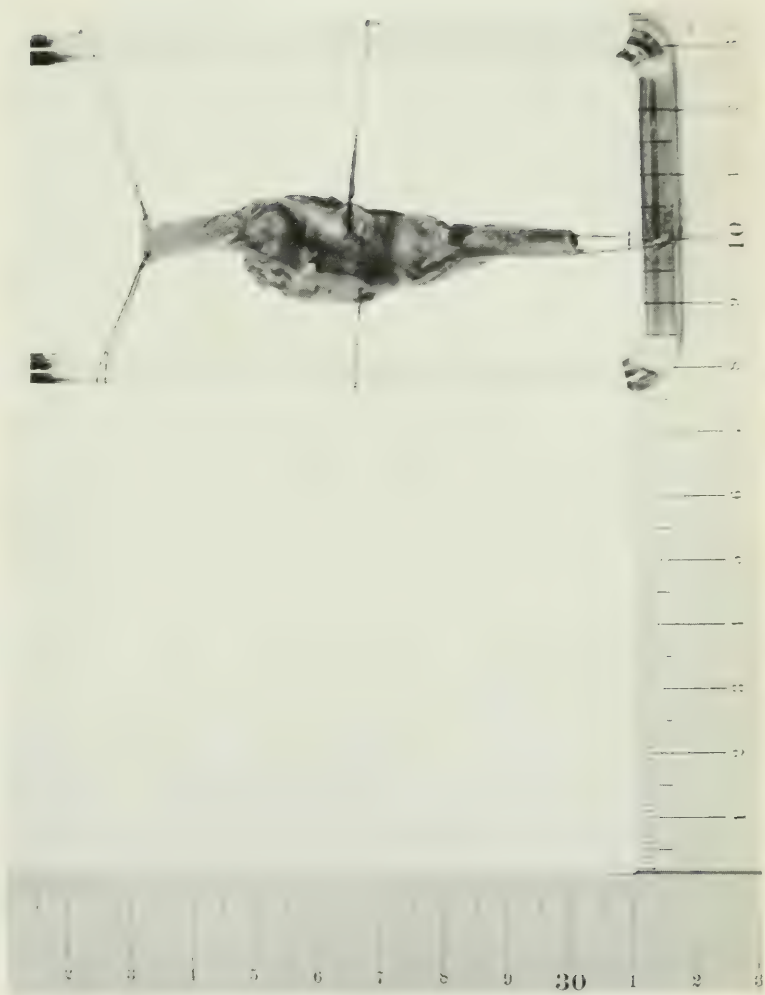


FIG. 8.—Dog 163, donor. Dog 164, black and white coon, mongrel host. Homotransplant, March 19, 1914. Specimen removed April 23. Gland shows partial absorption. Carotid has smooth intima. No thrombosis.

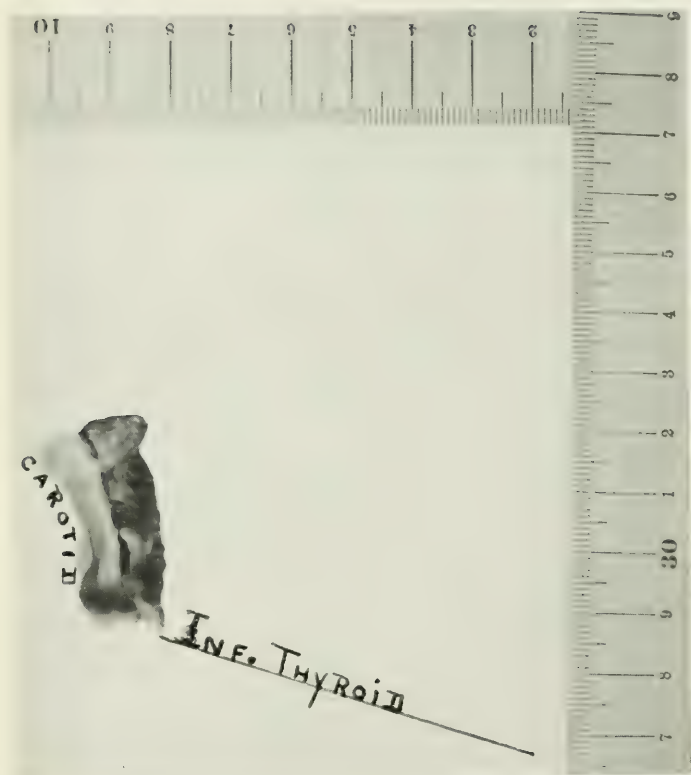


FIG. 9.—Dog 156, black and white bull, donor. Dog 157, mongrel host. Homotransplant of thyroid, March 16, 1914. Microscopic report—partial necrosis; no thrombosis.



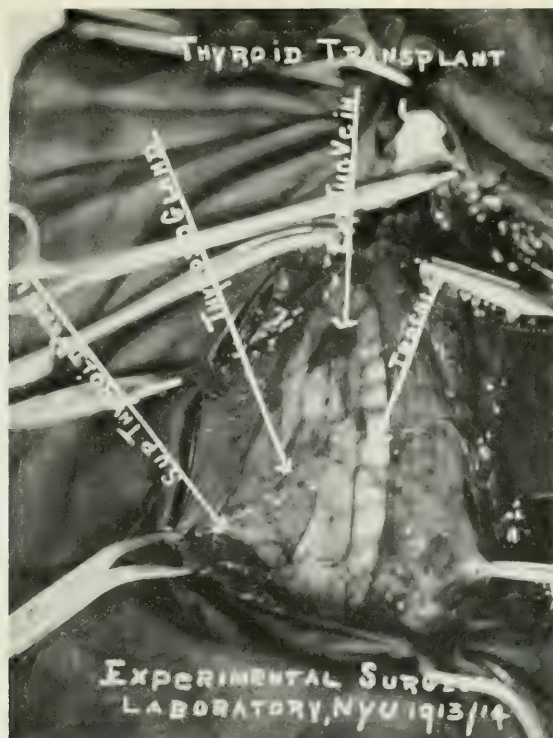


FIG. 10.—Exposure of thyroid body.

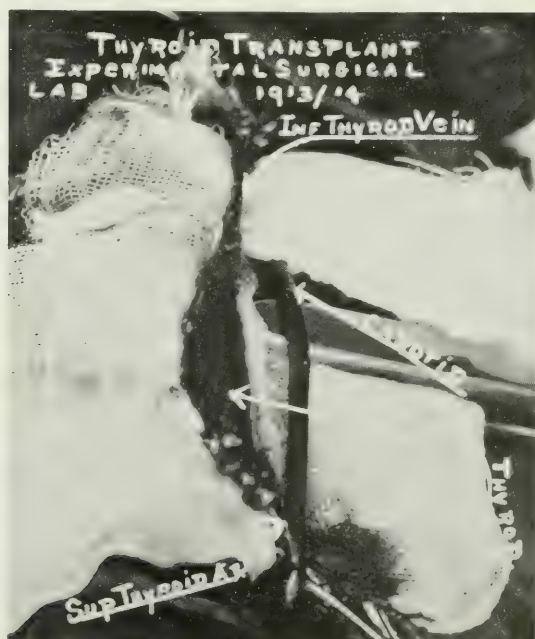


FIG. 11.—Thyroid isolated with vessels ready for removal.

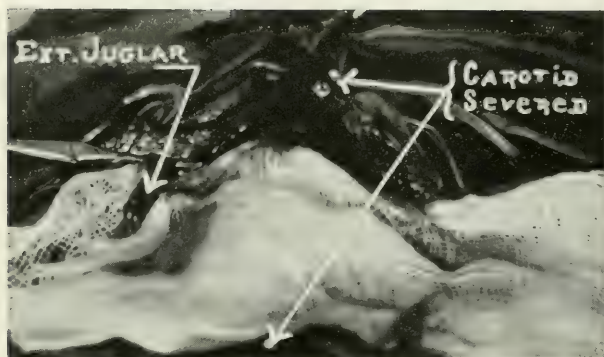


FIG. 12.—Carotid and external jugular of host prepared for reception of transplant.

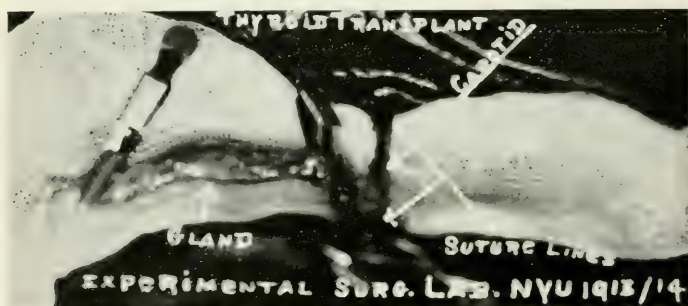


FIG. 13.—Carotid suture completed. Serrefines on thyroid vessels to prevent contamination of operative field.

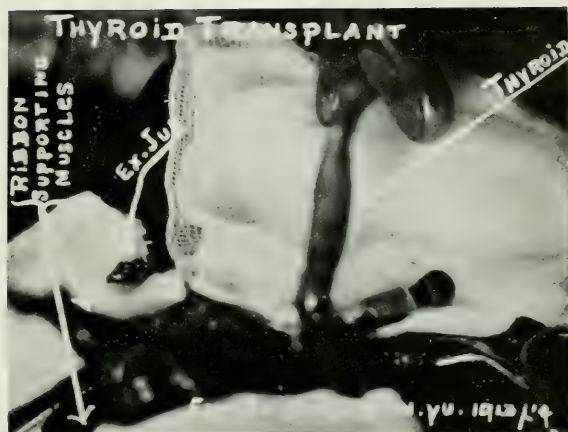


FIG. 14.—Muscles in front of trachea tunneled and raised to admit transplant.



FIG. 15.—Suture of thyroid end-to-end with external jugular of opposite side, completing transplantation.









## FERMENT DIAGNOSIS (ABDERHALDEN) FOR CANCER<sup>1</sup>

BY CHARLES GOODMAN, M.D., F.A.C.S.

AND

SAMUEL BERKOWITZ, M.D.

NEW YORK

SEVERAL thousand tests by dialysis after the method described by Emil Abderhalden and his co-workers have now found their way into the literature. While conclusive evidence of the merits of the test are substantiated by some authors, there are others who up to the present time have not been convinced of the reliability of the test in their hands and therefore question its practicability for clinical purposes. A critical review of the reports of some of these writers makes it apparent that all the details of the technique described and laid down by Abderhalden have not been mastered and complied with. The technique is intricate, and the outcome of the test depends upon the scrupulous observance of each and every detail, however minute.

Some of the earliest workers have improved their results by acquiring a corrected technique from Abderhalden or from one of his pupils, and until the details of the test have become simplified the most reliable statistics of the dialysis test will necessarily be derived from those who have received such instruction.

That the action in this test is due to blood-ferments was shown in 1909 by Abderhalden, working with Pincussohn and Weichert.<sup>2</sup> Abderhalden was guided by his belief that the presence of a foreign substance in the circulation is conducive to the production of antagonistic or protective bodies. That this holds true not only in pregnancy but also in other conditions has been shown by many observers, and we find that syphilis, brain abscess, mania, Basedow's disease, and cancer are among the diseases which are readily diagnosed by this method.

Recently we reported that we had found in the blood following the transplantation of the thyroid gland a ferment which was capable of digesting suprarenal.

In a series of cases of malignancy we were able to obtain 30 reactions out of 33 cases in which the results corresponded to operative, post-

<sup>1</sup> From the Physiological Chemical Laboratory, Beth Israel Hospital, and the Department of Physiological Surgery of New York University.

<sup>2</sup> Hoppe, Seyler's Ztschr., 1909, No. 61.

mortem and clinical findings. In the accompanying table one case of carcinoma was not diagnosed and one negative case was diagnosed as a sarcoma.

The imperative precautions asserted themselves with each step in this difficult procedure. Among those which should receive special mention are:

1. *Absolute asepsis* must be carried out in all the details of the test. *Especial cleanliness* must be observed in caring for the glassware.

2. The *substrate* (antigen) must be tested before each series of reactions, to avoid error from this source. Failure to macerate properly or divide the tissue in the preparation of the substrate seems to be a frequent source of error. For the purpose of maceration an ordinary meat chopper serves very well, since connective tissue usually becomes stringy and can easily be removed. The tissue should be divided into minute pieces, and not into pieces the size of a silver quarter or a bean as noted by other writers, for the point has been emphasized by Abderhalden that unless the tissue has been minutely divided before boiling it cannot be entirely freed from blood.

3. The *serum* must always be centrifuged until no red blood-corpuscles are visible after centrifuging for five minutes. Discolored serum is always discarded as valueless, as it usually gives positive results in negative cases.

4. Great care should be used in handling that part of the *thimble* which will take part in the dialysis. The thimbles used in our tests had been certified at Halle and were repeatedly tested.

The ninhydrin test is so delicate that only scrupulous care in handling the thimbles will avoid reaction due to perspiration or bacterial contamination. *Blowing* the water from the wash bottle, even with great precaution, may contaminate it with small amounts of saliva sufficient to produce conflicting results.

In conclusion one is competent to perform the tests only when such skill is acquired that negative cases are diagnosed as negative.

# FERMENT DIAGNOSIS (ABDERHALDEN) FOR CANCER

## ABDERHALDEN REACTION IN CANCER

Case Number	ccm. Serum Each Test	Time of Dialysis (hours)	Serum — Control	Serum + Carcinoma	Serum + Sarcoma	Serum + Placenta	Serum + Stomach	Serum + Artery	Serum + Pancreas	Serum + Adrenal	Clinical Diagnosis	Remarks
D. 10	1.0	18	0	++	0	0	—	—	—	—	Recurrent carcinoma breast.	Post-mortem.
M. 11	1.0	18	0	++	0	—	—	—	—	—	Carcinoma intestines.	Operated.
M. 12	1.0	20	0	++	0	—	—	—	—	—	Carcinoma breast.	Post-mortem.
M. 13	1.0	18	0	++	0	—	—	—	—	—	Retroperitoneal sarcoma.	Marked cachexia.
B. 14	1.5	18	0	++	0	—	—	—	—	—	General carcinomatosis.	Carcinoma, stomach, op.
B. 15	1.5	18	0	++	0	—	—	—	—	—	Tumor, abdomen.	Hydrocele fluid.
B. 16	1.0	16	0	++	0	—	—	—	—	—	Sarcoma testes.	Refused exploration.
B. 17	1.5	20	0	++	0	—	0	—	—	—	Carcinoma liver.	Section typical.
M. 18	1.0	24	0	++	0	—	—	—	—	—	Carcinoma femur?	+ Wassermann.
M. 19	1.0	24	0	++	0	—	—	—	—	—	Carcinoma uterus?	Operated.
M. 20	1.0	24	0	++	0	—	—	—	—	—	Carcinoma breast.	Ascitic fluid; post-mortem.
M. 31	1.5	24	0	++	0	—	—	—	—	—	Retroperitoneal sarcoma.	Blood serum.
M. 32	1.5	16	0	++	0	—	—	0	—	—	Retroperitoneal sarcoma.	4 years; no recurrence.
P. 1	1.0	24	0	++	0	—	—	—	—	—	Post-op., carcinoma breast.	
P. 2	1.0	20	0	++	0	—	—	—	—	—	Recurrent carcinoma breast.	
P. 3	1.5	18	0	++	0	—	—	—	—	—	Carcinoma stomach and liver.	
P. 4	1.0	20	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operated.
P. 5	1.0	24	0	++	0	—	—	—	—	—	Carcinoma recti.	Operated.
P. 6	1.5	20	0	++	0	—	—	—	—	—	Carcinoma recti.	Refused operation.
M. 33	1.5	20	0	++	0	—	—	—	—	—	Carcinoma liver.	Post-mortem.
M. 34	1.0	24	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operated.
P. 4	1.5	16	0	++	0	—	—	—	—	—	Carcinoma breast.	Operated.
P. 43	1.0	24	0	++	0	—	—	—	—	—	Carcinoma liver.	Refused operation.
B. 44	1.5	24	0	++	0	—	—	—	—	—	Carcinoma recti.	Refused operation.
B. 45	1.5	24	0	++	0	—	—	—	—	—	Carcinoma liver.	Operated.
B. 50	1.0	24	0	++	0	—	—	—	—	—	Carcinoma breast.	Ascitic fluid; post-mortem.
M. 35	1.5	24	0	++	0	—	—	—	—	—	Carcinoma liver.	Refused operation.
B. 51	1.5	24	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operation.
B. 52	1.5	24	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operation.
B. 53	1.5	24	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operation.
B. 54	1.5	24	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operation.
B. 55	1.5	24	0	++	0	—	—	—	—	—	Carcinoma pancreas.	Marked jaundice; refused operation.
B. 57	1.0	24	0	++	0	—	—	—	—	—	Carcinoma stomach.	Operation.
P. 1	1.0	18	0	++	0	—	—	—	—	—	Carcinoma recti.	Operation.





## THE ABDERHALDEN REACTION IN MALIGNANT TUMORS, PREGNANCY, AND ANGIOSCLEROSIS

REPORT OF A YEAR'S WORK<sup>1</sup>

BY CHARLES GOODMAN, M.D., F.A.C.S., NEW YORK  
Clinical Professor of Surgery, New York University

AND

SAMUEL BERKOWITZ, M.D., NEW YORK  
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WHILE I was in Goettingen working on the problem of the transplantation of organs under Prof. Hermann Stich, we succeeded in transplanting thyroids and spleens in dogs by the aid of blood-vessel suture. Our object was to determine a method of overcoming those biochemical differences in animals which are responsible for autolysis and the eventual absorption of the transplant. At the suggestion of Professor Stich, I went on to Halle to study under Professor Abderhalden his method of detecting protective ferments. Abderhalden proposed that we should begin by transplanting thyroid glands in dogs with a view of determining by dialysis which organs of the body were susceptible to insult following such transplantations.

I had brought to America a complete equipment for the test such as is used at the Halle Laboratory. The technique of the transplantations consisted in restoration of the normal circulation as far as possible by blood-vessel suture. The details of these experiments were published in the *Annals of Surgery*, 1915. In an article published in *SURGERY, GYNECOLOGY AND OBSTETRICS*, December, 1914, we reported our first results of the diagnosis of malignancy with the Abderhalden test. A review of the literature of 1914 and the early part of 1915 shows many conflicting reports, and a critical glance at its contents seems advisable in view of the importance of the test for the early diagnosis of malignant tumors.

Boldt reports 43 cases of complicated pregnancy. In 28 the clinical diagnosis of pregnancy was made. The reaction was correct 27 times and incorrect once. In 6 cases the clinical diagnosis was doubtful

<sup>1</sup> From the Physiological Surgical Research Laboratory, New York University, and the Laboratory of Physiological Chemistry, Beth Israel Hospital.

and the reaction proved correct in 5 and wrong in 1. None of these women were pregnant. In 6 other positively non-pregnant women, the Abderhalden reaction was weakly positive 4 times; in 1 the reaction was made just prior to menstruation. In 2 of the women the reaction was negative; that is, correct. In 3 cases extra-uterine pregnancy was suspected. The diagnosis in 2 of these was negatived by the reaction, which proved correct. The third case was verified as having a tubal gestation in the course of abortion, but the reaction was negative. Boldt concluded that the Abderhalden test was no more than an aid to diagnosis, but in doubtful cases it was a very valuable aid.

Echols carried out the test on 95 women, 70 of whom were known to be pregnant. The pregnant women gave positive reactions. About 12 per cent of non-pregnant individuals gave positive reactions, including several patients just operated on for acute or chronic appendicitis, pus tubes, fibroids, and ovarian cysts. Echols concluded that the dialysis test for pregnancy was of value chiefly in a negative sense; that is, if a woman failed to give a positive reaction, she was not pregnant. If, on the other hand, she gave a positive reaction she was probably pregnant. Echols also criticized the use of parchment tubes or thimbles on the ground that their permeability to peptones and amino-acids became altered by boiling, which is the only method of sterilizing them perfectly.

Schwarz reported 41 cases known to be pregnant which gave positive reactions and 30 cases known to be not pregnant which gave negative reactions. Schwarz is a believer in the strict specificity of cancer and pregnancy ferments. In 5 cases of cancer examined, the cancer sera gave strong reactions with cancer albumin and faint reactions with placental albumin; while the pregnant sera gave strong reactions with placental albumin, and weak reactions with cancer albumin. Schwarz ascribed the faint reactions to poorly prepared albumins.

Wohl concluded from his own 22 cases of pregnancy, in all of which a positive reaction was obtained, and from the review of all the literature up to the first of 1914, that the reaction for pregnancy stood on the same level as Wassermann's for syphilis; i.e., the reaction was positive in 80 to 90 per cent of the cases.

Wohl predicted a great future for the test for further research in pathology and therapeutics and cited 14 cases of epilepsy in which he found that cases which had progressed to the stage of dementia showed a ferment splitting up brain and testicle; serum of 2 of these cases showed cleavage of thyroid tissue as well. Furthermore, 3 patients

## THE ABDERHALDEN REACTION

who had had an attack a few hours before the blood was taken, reacted against brain and testicular tissue. He did not feel justified in drawing conclusions from the few cases he observed, but believes that Abderhalden's reactions will prove of great benefit in throwing more light upon the etiology as well as the prognosis of epilepsy. He also reported 2 cases of cancer in which the positive reaction was confirmed by operations.

Ball had correct reactions in 27 cases of tumors clinically or suspiciously malignant and in 22 non-malignant cases. There were three errors in positive reactions which Ball could not explain. He agreed with Frank and Heimann that certain pathological conditions such as myomata of the uterus, metritis and endometritis occasionally give a positive malignant reaction when not expected. Ball believes that poorly prepared substrata explained practically all of his erroneous findings, that bad thimbles came second, and that until further work perfected the technique, a clean-cut negative reaction carried much more weight than a positive one. Ball added that the association of this test with the bismuth meal and colonic injection made the strongest combination now at our command in the diagnosis of gastro-intestinal diseases.

Levin used adenocarcinoma of the breast tissue and obtained serum from 13 cases of carcinoma, 4 cases of sarcoma, 12 cases of pulmonary tuberculosis, and 8 cases of light nervous ailments. In the 13 carcinoma cases, 12 were positive and 1 negative. The sarcoma cases were all positive. Of the 12 tuberculous cases, 5 were positive and 7 negative, and of the last series, 4 were positive and 4 negative. Levin concluded that, while the test is more frequently positive in carcinoma, it could not be considered actually specific, since the same ferments seem to appear in the serum of non-carcinomatous individuals. He believed that the proteid substance which the ferments split up must be made to be more clearly specific and the test itself must be finer and not dependent on the behavior of the dialyzer. Levin finally remarked that for the present the method belongs to the research laboratory and not to the clinic.

R. St. Leger Brockman reported 25 cases of carcinoma and 20 cases in which carcinoma could be excluded beyond reasonable doubt. The test was positive in all 25 carcinoma cases and negative in the controls. One error in a control case was probably due to incubation lasting only 16 hours. Brockman believed his evidence sufficient to conclude that the test was specific for cancer.

J. Bauer had correct results in 8 carcinoma cases, but in 30 non-

carcinomatous cases only half were negative. These cases were stomach patients with gastric ulcer and achylia gastrica. Bauer concluded that the technique of the test was insufficiently developed, but he believed that we are at the beginning of the rich harvest promised by the Abderhalden basic ferment theory.

Oeller and Stephan have constructed a new apparatus for the boiling of the dialysate to facilitate strict asepsis and to enable the worker to boil very rapidly a number of tests, obtaining at the same time an even boiling temperature.

Abderhalden in his Leyden lecture stated that the test was correct in 50 carcinoma cases and that sarcoma and carcinoma could be sharply distinguished. Abderhalden added that about 600 cases of pregnancy correctly diagnosed by his test proved that only experimental errors lead to erroneous diagnoses.

Bornstein reported that he had positive results in 70 per cent of many of his carcinoma tests but in others only from 40 to 50 per cent. He concluded that if the reaction was positive, carcinoma is certainly present, but if it is negative the patient might nevertheless have a carcinoma. Bornstein thought that when the blood was pressed out of the preparation the greatest part of the cancer foci was also pressed out, and the preparation became too weak.

Mayer reported 18 carcinoma cases which had positive results, and gave his interesting experiments with the test on the ductless glands.

Oeller and Stephan attributed all errors to the dialyzers and their permeability, and required two tests for a positive result and several non-specific organ substrata for the specificity control.

De Waele found that thymol added to the serum and to the thimble wash aids in obtaining correct results.

Plant proved in experiments on 40 psychiatric cases that an increase of the proteolytic ferments in the dialysate could be caused by the presence of an organic, non-proteolytic substance, and that this factor of absorption must be reckoned with as a possible source of error. This has also been pointed out by Abderhalden on page 190 of the third German edition of *Abwehrfermente*.

Epicum had 98 per cent correct results in 51 of his observations.

Kämmerer, Clausz and Dieterich had difficulties in their twelve series of experiments on ductless glands and carcinomata which they ascribe in great part to the inequality of the thimbles.

Singer in five series of experiments and in the verifications of the experiments of Hilner and Petri arrived at the conclusion that the



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strict specificity of the test has not yet been proved and that the dialysis method was not yet ready for general use.

Guggenheimer believed that the divergence of results of the different authors in respect to the specificity of the ferments in the carcinoma and organ diagnosis might be due to the occasional factor of an associate destructive ferment and also to the ground tissue of the tumor, as occasionally uterus carcinoma might be digested by the serum of non-carcinomatous genitally diseased patients. Guggenheimer also pointed out that an organic injury involved secondary disorders of other organs, the functional disturbances of which are indicated by the presence of the corresponding serum ferments. He concluded, however, that the specificity was far-reaching.

Allmann had success in pregnancy diagnosis but dubious results in 12 carcinoma cases.

Heimann and Fritsch reported 34 reactions in carcinomata which were afterward proved by histological tests. They believed that when the Abderhalden test is perfected in technique and that with the exclusion of undesirable material a carcinoma might even be diagnosed from two to three weeks before its beginning, and thus the carcinoma prognosis might be rendered immeasurably more favorable.

Ball reported 51 cases. Of the 6 cases clinically malignant the reaction was positive. Of the suspiciously malignant conditions examined, 20 of the 28 gave positive reactions, which were verified by röntgenograms in 3 persons, post-operative microscopical section in 10 instances, and definite subsequent histories in 7 cases.

Benech had correct results in 20 cancerous cases and 25 control cases.

Csépai attributed his unsatisfactory results to errors in technique, especially to faulty thimbles, and believed that the test had great value especially in the diagnosis of disorders of internal secretion.

Lampe and Paregger pointed out that the substrata must be prepared, tested, and handled with the greatest care and that the verdict as to the specificity of the ferments depends entirely upon them.

Fritsch believed that the carcinoma test will only be reliable in the hands of experienced investigators working in a large laboratory.

Berghausen had successful reactions in 41 tests, except that the serum of 2 patients suffering from carcinoma of the uterus failed to digest placental tissue and that the serum of 1 pregnant woman failed to digest epithelioma tissue, while that of another digested it. Oettinger, Fiessinger, and Pierre Marie reported that in their 63 cases the reaction was positive in two-thirds of the cancer cases and negative



## ABDERHALDEN REACTION IN CANCER

Case Number	Referred By	Cm. Serum each Test	Time of each Test (hrs.)	Serum Control	Serum + Carcinoma	Serum + Sarcoma	Serum + Placenta	Serum + Stomach	Serum + Artery	Serum + Pancreas	Serum + Adrenal	Serum + Large Gut	Clinical Diagnosis	Remarks
D. 10	Dr. M. Fishberg	1.5	18	0	+	0							Recurrent carcinoma breast	Adenocarcinoma.
M. 11	Montefiore Hosp.	1.5	18	0	+	0							Carcinoma intestines	Post-mortem.
M. 12	Montefiore Hosp.	1.0	20	0	+	0							Carcinoma breast	Adenocarcinoma.
M. 13	Montefiore Hosp.	1.0	18	0	0	+++							Retropitoneal sarcoma	Post-mortem.
B. 14	Dr. L. J. Ladinski	1.5	18	0	+	0	0						General carcinomatosis	Marked cachexia.
B. 15	Dr. C. Goodman	1.5	20	0	+++	0							Tumor, abdomen	Adenocarcinoma, stomach, op.
B. 16	Dr. C. Goodman	1.0	16	0	0	+							Sarcoma, testes	Hydrocele fluid
B. 17	Dr. A. A. Himowich	1.5	20	0	+	0		0					Carcinoma liver	Refused exploration.
M. 18	Montefiore Hosp.	1.0	24	0	0	++							Sarcoma femur	Section typical.
M. 19	Montefiore Hosp.	1.5	24	0	0	0	+						Carcinoma uterus (?)	+ Wassermann.
M. 20	Montefiore Hosp.	1.0	24	0	+	0	0						Carcinoma breast	Operated.
M. 31	Montefiore Hosp.	1.5	24	0	0	++							Retropitoneal sarcoma	Ascitic fluid; post-mortem.
M. 32	Montefiore Hosp.	1.5	16	0	0	+			0				Retropitoneal sarcoma	Blood serum.
P. 1	Dr. C. Goodman	1.0	24	0	+	0							Post-op.; carcinoma breast	4 years; no recurrence.
P. 2	Dr. C. Goodman	1.5	20	0	+	0							Recurrent carcinoma breast	Adenocarcinoma.
B. 41	Dr. R. Lewisohn	1.0	18	0	+	0							Carcinoma stomach and liver	Operated.
P. 3	Dr. L. Friedman	1.0	20	0	++	0				0			Carcinoma stomach	Operated.
B. 42	Dr. A. A. Himowich	1.0	24	0	+	0							Carcinoma stomach	Refused operation.
M. 33	Montefiore Hosp.	1.5	20	0	+	0					+		Carcinoma recti	Post-mortem.
M. 34	Montefiore Hosp.	1.0	24	0	+	0*							Carcinoma liver	Post-mortem.
P. 4	Dr. C. Goodman	1.5	20	0	+	0							Carcinoma stomach	Operated.
B. 43	Dr. L. J. Ladinski	1.5	16	0	+	0							Carcinoma breast	Operated.

Case Number	Referred By	Cm. Serum each Test	Time of Dialysis (hrs.)	Serum Control	Serum + Carcinoma	Serum + Sarcoma	Serum + Placenta	Serum + Stomach	Serum + Artery	Serum + Pancreas	Serum + Adrenal	Serum + Large Gut	Clinical Diagnosis	Remarks
B. 44	Dr. D. Robinsohn	1.0	24	o	+	o							Carcinoma liver	Refused operation.
B. 45	Dr. C. Goodman	1.5	24	o	+	o							Carcinoma recti	Refused operation.
B. 50	Dr. C. Goodman	1.0	24	o	o	o							Carcinoma breast	Operated.
M. 35	Montefiore Hosp.	1.0	24	o	+	o							Carcinoma liver	Ascitic fluid; post-mortem.
B. 51	Dr. C. Goodman	1.5	24	o	+	o		+					Carcinoma stomach	Refused operation.
B. 52	Dr. A. A. Himowich	1.5	24	o	+	o			o				Carcinoma stomach	Operation.
B. 53	Dr. C. Goodman	1.5	24	o	+	o		+					Carcinoma stomach	Operation.
B. 54	Dr. A. A. Himowich	1.5	24	o	+	o			o				Carcinoma stomach	Operation.
B. 55	Dr. D. Robinsohn	1.5	24	o	+	o							Carcinoma stomach	Operation.
B. 57	Dr. D. Robinsohn	1.0	24	o	+	o							Carcinoma pancreas	Marked jaundice; refused operation.
P. 5	Dr. L. J. Ladinski	1.0	18	o	+	o	o						Carcinoma recti	Operation.
V. 101	Dr. G. D. Stewart	1.0	24	o	+	o							Carcinoma cervix	Post-operative 7½ years.
V. 102	Dr. G. D. Stewart	1.0	24	o	+	o							Carcinoma stomach	Post-operative.
V. 103	Dr. G. D. Stewart	1.0	24	o	o	o							Tumor, breast	Age 51 years; mass in breast.
B. 104	Dr. G. A. Friedman	1.0	24	o	+	o							Carcinoma stomach	Post-operative.
B. 105	Dr. L. B. Meyer	1.0	24	o	+	o							Carcinoma liver	Post-operative.
V. 106	Dr. G. D. Stewart	1.0	24	o	+	o							Carcinoma pancreas	Clinically.
V. 107	Dr. G. D. Stewart	1.0	24	o	+	o							Carcinoma breast	Recurrence.
M. 111	Montefiore Hosp.	1.5	16	o	+	o							Carcinoma recti	Adenocarcinoma.
P. 112	Dr. J. T. Lynch	1.5	24	o	+							+	Carcinoma stomach	Under observation.
M. 113	Montefiore Hosp.	1.5	48	o	o	+++							Multiple myeloma	Bence-Jones Albuminuria.

## ABDERHALDEN REACTION IN CANCER—Continued

Case Number	Referred By	Cm. Serum each Test	Time of Diagnosis (hrs.)	Serum Control	Serum + Carcinoma	Serum + Sarcoma	Serum + Placenta	Serum + Stomach	Serum + Artery	Serum + Pancreas	Serum + Adrenal	Serum + Large Gut	Clinical Diagnosis	Remarks
B. 114	Dr. A. A. Himowich	1.5	48	0		+							Retroperitoneal sarcoma	Clinically.
B. 115	Dr. A. A. Himowich	1.0	24	0	+	0						0	Carcinoma lungs	Post-mortem.
P. 117	Dr. J. T. Lynch	1.5	18	0	+	0							Carcinoma stomach	Same as No. P. 112.
P. 118	Dr. C. Goodman	1.0	24	0	+	0						+	Carcinoma recti	Operated.
U. 120	Dr. G. D. Stewart	1.0	18	0	+	0						+	Carcinoma large gut	Clinically and X-ray.
P. 121	Dr. J. T. Lynch	1.0	18	0	+	0							Carcinoma stomach	Under observation.
B. 122	Dr. H. M. Silver	1.0	18	0	+	0							Carcinoma stomach	Operated.
U. 124	Dr. G. D. Stewart	1.0	17	0	0	0							Epithelioma esophagus	Substrate: adenocarcinoma.
U. 125	Dr. G. D. Stewart	1.0	17	0	+								Carcinoma cecum	Operated.
U. 126	Dr. G. D. Stewart	1.0	17	0	+								Carcinoma cecum	Recurrence.
U. 127	Dr. G. D. Stewart	1.0	17	0	+								Carcinoma pancreas	Operated.
U. 134	Dr. G. D. Stewart	1.5	24	0	+	0						0	Carcinoma lip	Operated.
B. 136	Dr. C. Goodman	1.0	24	0	0	+							Endothelioma larynx	Recurrence.
P. 137	Dr. L. Friedman	1.0	24	0	+								Carcinoma uterus	Post-operative.
P. 139	Dr. L. Friedman	1.0	24	0	+	0							Carcinoma cervix	Post-operative.
B. 142	Dr. C. Goodman	1.0	24	0	+	0							Carcinoma recti	Post-operative.
B. 143	Dr. D. Robinsohn	1.0	24	0	0	+							Sarcoma glands	Typical pathology.
B. 145	Dr. L. J. Ladinski	1.0	24	0	+	0							General carcinomatosis	Clinically.
U. 146	Dr. G. D. Stewart	1.5	18	0	+	0							Abdominal tumor	Under observation.
B. 250	Dr. Isadore Seff	1.5	24	0	+	0						+	Carcinoma liver	Operation.
B. 251	Dr. Isadore Seff	1.5	24	0	+	0						+	Carcinoma bladder	Inoperable; cystoscopy.

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in one-third. In the non-cancerous affections the reaction was positive in one-third of the cases and negative in two-thirds. The authors concluded that the test was only very little, if at all, superior to the other laboratory methods.

Bisgaard and Korsbjerg did not consider the ninhydrin method delicate enough to ascertain the protease action and reported unsatisfactory results from their experiments.

Fritsch remarked that when a number of parallel tests were made, the possibility of errors from the thimbles was of course decreased, but holds to his original opinion that the test may be used only as an adjunct.

Keitler and Lindner proved that exposure to X-rays has a retarding influence on the formation of ferments in animal experiments.

Schumkowa-Trubina found that the test was positive in about 95 per cent of the cancer cases, and the greater the homology between the substrate and the tumor of the case tested, the more frequent were the successful results.

Otto and Blumenthal had conflicting results and did not think the test was suitable for clinical purposes.

Parodi and Vidoni had conflicting results, and were extremely pessimistic as to the specificity of the test for pregnancy or for malignancy.

Gavrinsky believed that the negative results of the test in suspected malignancy spoke strongly against the existence of such conditions.

Biehn reported that the results of his experiments on animals regarding the protective ferments had borne out Abderhalden's statements as to their specific nature. He believed that greater reserve in reporting successful results was necessary and that we demand too much of the test, forgetting that all laboratory findings must be taken only as additional symptoms that serve to confirm or deny the other clinical signs.

Falls agreed in the main with Biehn's opinion of the value of the test as corroborative evidence, but was more pessimistic.

We are inclined to believe that a part of the unsuccessful results obtained by the authors should be ascribed to technical errors. In some of the instances these have been caused by poorly directed efforts to simplify an intricate and delicate technique even before the workers have mastered the test as described by Abderhalden in his book, *Abwehrfermente des tierischen Organismus*, 1913, which has now been translated into English.



In our work during the past twelve months the results have been more uniformly in accord with the research at the Halle Laboratory of Professor Abderhalden. He had made in all 334 dialysis tests, and of this number 27 were discarded because the blood was contaminated or else was withdrawn too soon after eating.

In cancer we have examined the blood of 64 patients. We obtained positive reactions in 58. In all of the 58 cases the positive diagnosis of malignancy was confirmed later by clinical, operative, or post-mortem evidence. Of the remaining 6 cases, 3 are still under observation.

We believe that the Abderhalden dialysis reaction as a corroborative test for malignancy has equal importance with any of the other recognized clinical laboratory methods of serum diagnosis.

We desire to repeat with emphasis that negative results are even more valuable than positive results.<sup>1</sup> To verify our positive findings and avoid discrepancies we invariably used a thimble containing serum alone. A positive reaction with ninhydrin in the control dialysate was attributed to errors in our technique, which arose either from contamination while the specimen was being obtained or in the handling of the thimbles. These were therefore discarded. We did not use blow wash bottles on account of the danger of contamination from saliva, as saliva gives a positive reaction with ninhydrin in parts of 1:1,000,000 (Abderhalden).

Our cases of malignancy consisted of the following: 16 with carcinoma of the stomach; 9 with carcinoma of the breast; 10 with carcinoma of the intestines; 6 with carcinoma of the liver; 4 with carcinoma of the uterus; 3 with carcinoma of the head of the pancreas; 1 with carcinoma of the lungs; 2 with general carcinomatosis; 1 with epithelioma of the lip; 1 with carcinoma of the bladder; 1 with multiple myelomata; 1 with an abdominal tumor; 1 with carcinoma of the œsophagus; 1 with endothelioma of the larynx; 4 with retroperitoneal sarcoma; 1 with sarcoma of the testis; 1 with sarcoma of the femur; and 1 with sarcoma of the cervical glands. Of these cases, No. B. 16, a hydrocele of the tunica vaginalis, was diagnosed as a sarcoma; No. B. 50, a positive case of carcinoma of the breast, and No. U. 124, an epithelioma of the œsophagus, were diagnosed as negative.

In a large series of pregnancy tests, the results were uniformly satisfactory. In order to illustrate the value of the test as a factor in determining the course of procedure where the usual clinical symptoms

<sup>1</sup> Surg., Gynec. & Obst., 1914, xix, 797.



PREGNANCY WITH COMPLICATIONS

Case Number	Ccm. Serum Dilysis (Each Test)	Time of Dilysis (Hours)	Serum Control	Serum + Placenta	Serum + Thyroid	Serum + Stomach	Serum + Pancreas	Stage of Pregnancy	Remarks
P. 71	1.0	20	0	+	+		0	Third month	With glycosuria.
P. 72	1.0	20	0	+++					
D. 73	1.5	18	0	+			0	Ten weeks	
D. 74	1.5	24	0	++			+	Fifth month	Nausea and vomiting.
P. 75	1.0	24	0	++					With pulmonary tuberculosis.

ANGIOSCLEROSIS

Case Number	Ccm. Serum Dilysis (Each Test)	Time of Dilysis (Hours)	Serum Control	Serum + Artery	Serum + Brain	Serum + Adrenal	Clinical Diagnosis	Remarks
B. 260	1.0	24	0	0	0		Tertiary lues; cerebral complications	
M. 261	1.0	24	0	+	0		Paralysis agitans; arteriosclerosis	Blood pressure, 190.
M. 262	1.0	20	0	++	0		Arteriosclerosis	Age 74.
B. 263	1.5	24	0	+++		0	Angiosclerosis	One year after arteriovenous anastomosis. Placenta and serum also negative.
B. 264	1.5	18	0	+++		+++	Angiosclerosis	Post-operative.
B. 265	1.0	18	0	+	0	++	Angiosclerosis	Post-operative.
M. 266	1.5	24	0	++			Arteriosclerosis	Epilepsia.
P. 267	1.5	24	0	++		++	Angiosclerosis	Post-operative.

were not sufficient to form definite conclusions, we add the details of the following cases:

In No. P. 72, a multipara, age 39, her last pregnancy 17 years before, menstruation was regular until last menses six weeks prior to the examination which revealed a pelvic hæmatocele. The Abderhalden reaction was positive with placenta.

In patient No. P. 71, a woman about 20 years old, primipara, pregnant three months, the urine showed marked traces of glucose. An Abderhalden test gave a positive reaction with placenta and thyroid and a negative one with pancreas. Glycosuria disappeared at the termination of pregnancy.

Patient No. P. 73, an interesting case at the Presbyterian Hospital, was a young woman on whom left nephrectomy for renal tuberculosis had been performed by Dr. Blake at the Presbyterian Hospital prior to her marriage. After 18 months, the surgeons were of the opinion that she might safely marry, provided she had no children. A guinea pig injected with a catheterized specimen of her urine remained well for two months and at autopsy showed no tubercular lesions. Ten months after marriage, she went to see Dr. Whipple in regard to her menses, which she had noted were two weeks late. Two weeks later she developed morning nausea. At this time her urine contained more albumin than usual and there was a considerable amount of pus and blood. A week later, pelvic examination revealed no positive signs nor did her breasts show any changes of pregnancy. We then made an Abderhalden test with placenta substrate which was positive. As it was necessary for the pregnancy to be terminated, the attending physicians performed a curettage under gas-oxygen anæsthesia, and removed a fœtus estimated to be of ten weeks' development. She had a steady convalescence after one week of serious illness and was up and about in three weeks.

In a series of cases of angiosclerosis, we obtained positive reactions with artery and in several instances with adrenal substrata.

In the experimental tests on dogs we believe that our evidence in the foregoing cases substantiates the results of other writers who hold that the protective ferments show specificity in the Abderhalden dialysis reaction.

In a series of thyroid transplants we have been able in 17 instances out of 23 to show positive reactions with suprarenal and in 2 instances a positive reaction also with pancreas, but only 1 positive reaction with spleen. All of our specimens of blood taken from animals fol-

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lowing the transplantation of organs with the use of blood-vessel suture reacted positive with the substrate artery.

ABDERHALDEN REACTION FOLLOWING TRANSPLANTATION OF ORGANS

Dog Number	Cm. Each Test	Time of Dialysis (Hours)	Serum Control	Serum + Adrenal	Serum + Spleen	Serum + Pancreas	Serum + Pituitary Gland	Serum + Thyroid
214	1.0	20	0	+++	+			
180	1.5	24	0	+	0			
180	1.0	24	0	+	0			
191	1.0	24	0	+	0			
214	1.0	24	0	+		++		
282	1.0	24	0	+		+		
282	1.0	24	0	+				
282	1.0	24	0	+				
214	1.0	24	0	++				
282	1.0	24	0		0			
214	1.0	24	0				+	
269	1.0	24	0	0				
214	1.0	24	0			+		
214	1.0	24	0	+				+
268	1.0	24	0	0		+		
141	1.0	20	0	++	+			
114	1.5	24	0	+				
114	1.5	24	0	++				
114	1.5	24	0	0				
132	1.5	24	0	++				
164	1.5	24	0	+				
192	1.5	24	0	++				
242	1.5	24	0	+				

We conclude that the test is of great value in confirming clinical observations, and that those who rely upon laboratory tests alone for diagnosis are bound to be disappointed, not on account of the inferiority of the test but of its necessary limitations.

To those who kindly contributed specimens we desire to express our thanks.

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## HYDRONEPHROSIS

AN EXPERIMENTAL STUDY\*

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AND

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OF NEW YORK CITY

IN the course of a study of the causative factors of renal infection, the association of paralysis of the ureter and dilatation of the kidney pelvis and calyces was so frequent as to suggest experimental observations on hydronephrosis. The latter lesion may be defined as dilatation of the pelvis of the kidney by fluid attended by secondary dilatation and final obliteration of the calyces and by mechanical compression and atrophy of the parenchyma.

Clinicians<sup>7</sup> explain the etiology of hydronephrosis in assuming mechanical obstruction to the outflow of urine by foreign bodies, neoplasms, inflammatory exudates, and the like.

Wagner,<sup>9</sup> of Leipzig, describes the possible effects of traumatism to kidney and ureter. That traumatism gives rise to ureteral stricture or to peri-ureteral extravasation which may obstruct urine outflow and distend the kidney, he certainly affirms; that the intra-ureteral hemorrhage may coagulate and cause obstruction he faintly suggests. Ureters have been traumatized by ligation. They have been tied off experimentally as well as unwittingly. Experimentally "Guyon<sup>11</sup> and Albarran found congested kidney" after 57-70 hours of urethral ligation expressed by him in the following measurements:

Right kidney	P.M. cm.	A.M. cm.	Left kidney	P.M. cm.	A.M. cm.
Length.....	5.5	5.0	Length .....	5.8	5.5
Breadth.....	3.3	2.7	Breadth .....	4.0	2.8
Thickness .....	3.3	2.7	Thickness .....	4.0	2.9

Bradford<sup>5</sup> ligated the ureter for 11-40 days. He found the ureter always completely obstructed and the kidney invariably distended so that on incision at second operation 50-70 c.c. of urine was liberated. Most frequently, hydronephrosis resulted; in three cases out of twelve, pyonephrosis followed. Both Guyon's "congested kidney" and Brad-

\* Conducted at Laboratory of Experimental Surgery at New York University Medical School.

ford's hydronephrosis were transitory conditions associated with marked atrophy. Rayer avoids the association of complete obstruction and hydrourenal distention. Keen and Morris maintain that complete sudden obstruction brings about a rapid atrophy following a transitory distention. With this we agree. Experimentally both of a dog's ureters were stripped and one was ligated firmly at the ureterovesical junction. The animal lived for five days in a drowsy indolent state. At autopsy both kidneys were found hydronephrotic, the ligated ureter-kidney twice the size of the nonligated ureter-kidney. The measurements were as follows:

Right kidney	P.M. cm.	A.M.* cm.	Left kidney	P.M. cm.	A.M.* cm.
Length.....	9.0	6	Length .....	7.0	6
Breadth.....	6.0	4	Breadth .....	5.0	4
Thickness .....	4.0	2	Thickness .....	3.0	2

TABLE I

EFFECT OF STRIPPING URETER COMPARED WITH EFFECT OF STRIPPING AND LIGATING URETER

*Experimental Surgical Laboratory, N. Y. U. 1913-14*

Hydronephrosis

Dog No.]	Gross Findings †	Microscopical Findings	Cause of Death	Days of Life
146	Left: Hydronephrosis, slight Right: Hydronephrosis, slight	Diffuse glomerular and intertubular congestion Local congestion; parenchymula degeneration	Hydronephrosis	5

Obstructive inflammation of the urinary tract may be acute or chronic. Delbet<sup>8</sup> and others report ulcerative pyelitis or ureteritis following calculus irritation. Oertel<sup>10</sup> reports a singular inflammatory change in the kidney pelvis analogous to the connective-tissue hyperplasia in productive senile arteritis which permits distention under normal conditions of intrapelvic pressure.

Morris<sup>3</sup> reports many interesting anomalies of the ureter and the renal arteries obstructing urine delivery to the point of renal distention. Van der Bogert<sup>6</sup> reports a congenital type of hydronephrosis following aplasia of the ureter.

\* Estimate measurements.

† "Left" and "right" refer to animal and are reversely represented in table and in Fig. 8. Congestion is more marked in ligated ureter-kidney and degeneration has begun.



FIG. 1.—One of the steps in the technic of isolating and stripping of ureter, and irritating sup-  
positional ureteral nerve plexus.



FIG. 2.—Pyonephrosis following stripping of the ureter. Other kidney and ureter normal.

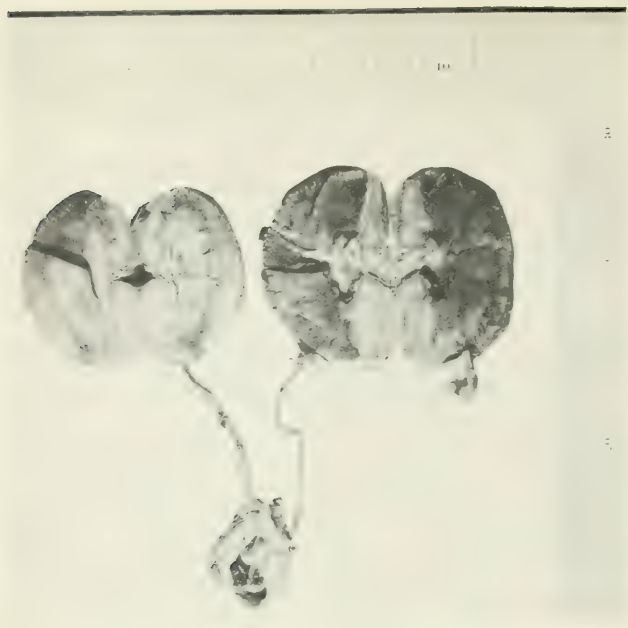


FIG. 3.—Dog No. 103. Hydronephrosis on right side following stripping of ureter; congested stage. Other kidney and ureter normal.

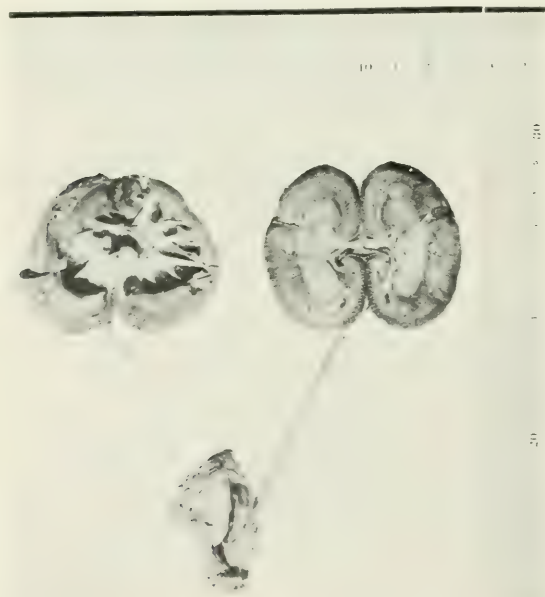


FIG. 4.—Dog No. 70. Hydronephrosis following stripping of ureter; dilated tubules stage. Other kidney and ureter normal.



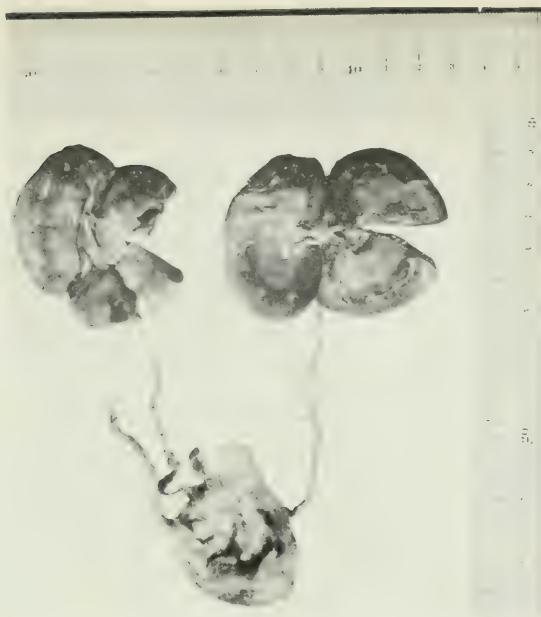


FIG 5.—Dog No. 17. Hydronephrosis following stripping of ureter shown on left side; dilated tubule stage. Other kidney and ureter normal.



FIG. 6.—Dog No. 54. Hydronephrosis and hydro-ureter following stripping of ureter; advanced stage. Other kidney and ureter normal.



FIG. 7. —Dog No. 69. Pyonephrosis following secondarily infected hydronephrosis after stripping of ureter; terminal stage. Other kidney and ureter normal.

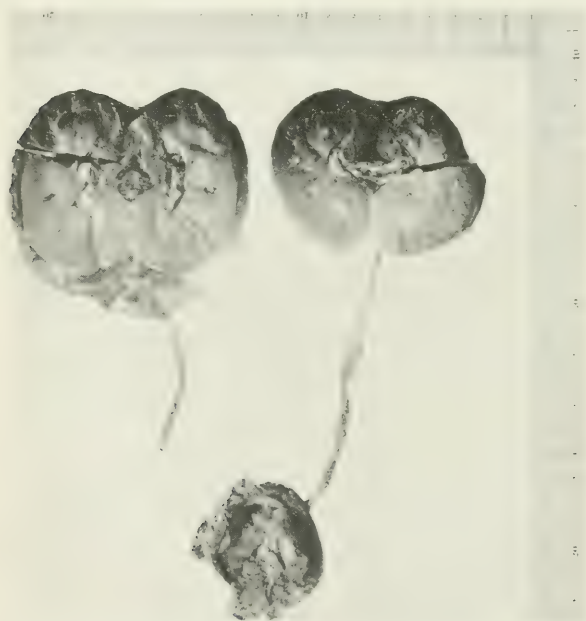


FIG. 8.—Dog No. 146. Hydronephrosis, both sides, produced on right by stripping of ureter and on left by ligation of ureter; congested stages. Notice perinephritic hemorrhage on left side.

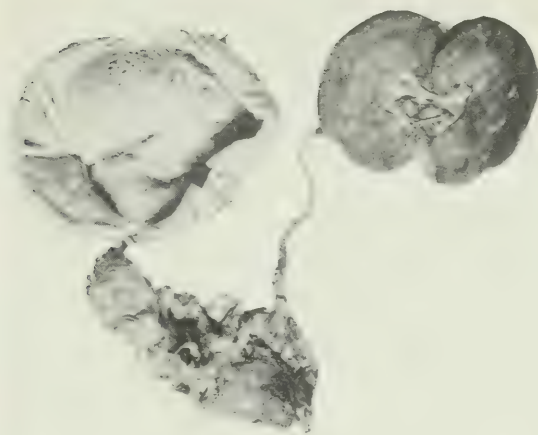


FIG. 9.—Dog No. 120. Pyonephrosis following stripping of ureter and circumcision of ureterovesical valve; advanced stage. Other kidney and ureter normal.



FIG. 10.—Dog No. 152. Hydronephrosis following ureteral calculus at junction of lower and middle thirds. Bladder shows vesical calculus.



FIG. 11.—Hydronephrosis following calculus at ureteropelvic junction of ureter. From clinical case.

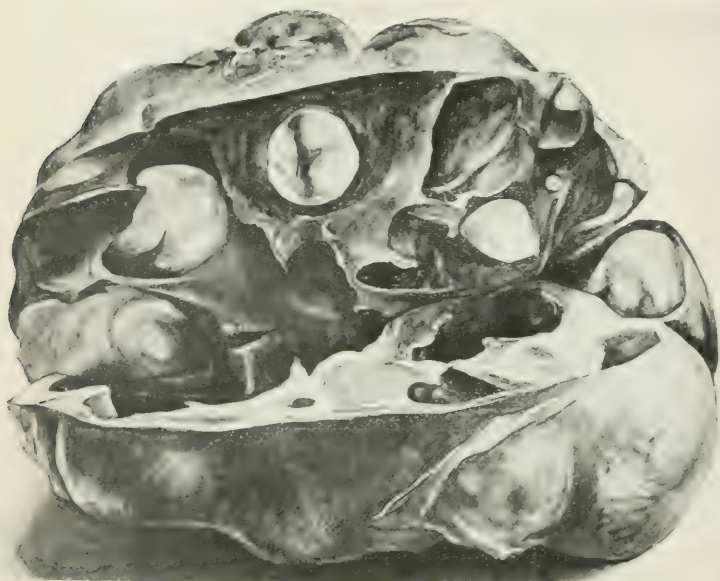


FIG. 12.—Hydronephrosis following calculus at ureteropelvic junction of ureter. Showing cut section.

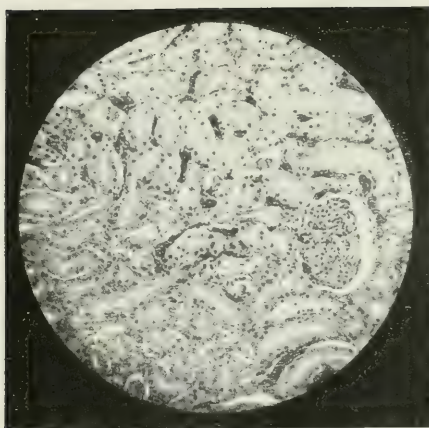


FIG. 13.—Dog No. 146. Showing intertubular and glomerular congestion occurring at the end of five days, following stripping of ureter.

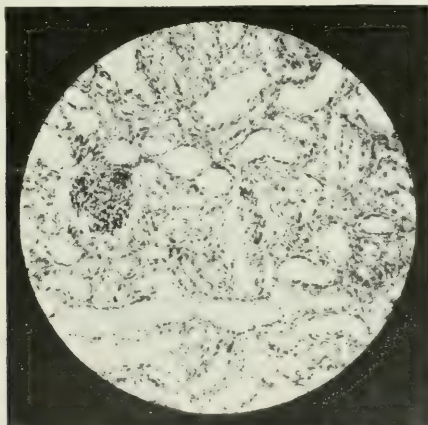


FIG. 14.—Dog No. 70. Showing dilated peripheral tubules from dilated tubules stage of experimental hydronephrosis.





## HYDRONEPHROSIS

Keen <sup>16</sup> and others enumerate tumors of the ureter and bladder among the causes of nephrectasia.

We offer for consideration the following: Physiologic or adynamic ureteral obstruction may give rise to distended kidney. To determine this we used dogs, after properly narcotizing with morphia and anæsthetizing with ether. In nine cases <sup>18</sup> the ureter was removed from its bed and stripped of every recognizable vessel nerve and fascial connection from kidney pelvis to bladder insertion, and in order to make sure it was absolutely freed from nervovascular connections through its course as well as to irritate the suppositional nerve plexus in the adventitia of the ureter, this organ was rubbed snugly with dry gauze throughout. It was then allowed to drop back into the abdominal cavity. In each case a cubical foreign body infected with autogenous colon bacilli and other organisms, and of such shape as not to cause valvular urethral obstruction as suggested by Draper and Braasch, was placed in the bladder through a mesoventrad incision, so that, as subsequent examinations of urine and bladder revealed, a permanent purulent cystitis was produced. The results were as follows:

TABLE II  
SHOWING EFFECT OF STRIPPING URETER <sup>18</sup>

Case No.	Gross Findings	Microscopical Findings	Cause of Death	Condition of Ureter	Bacteriological Findings	Days of Life
103	Hydronephrosis	Congestion	Intussusception	Patent	Coccus colon-like organ	7
70	Hydronephrosis	Dilated tubules	Hydronephrosis	Stenosed	Coccus colon-like organ	21
17	Hydronephrosis	Dilated tubules	Hydronephrosis	Patent	Coccus colon-like organ. No change in fixation test for colon	31
54	Hydronephrosis; hydro-ureter	Nephritis	Hydronephrosis	Patent	Culture omitted	25
69	Pyonephrosis	Purulent nephritis	Pyonephrosis	Stenosed	Coccus colon-like organism	29
21	Normal	Glomerular congestion	Perforation of bladder	Patent	No change in fixation test for colon	24
22	Parenchymatous degeneration	Parenchymatous degeneration	Peritonitis (technical)	Patent	No change in fixation test for colon	8
24	Interstitial nephritis	Productive nephritis	Pneumonia	Patent	Culture omitted	121
100	Hydronephrosis	Nephritis	Hydronephrosis	Stenosed	Culture	69

In each of the three cases designated "stenosed" the obstruction appeared to be organized blood within the ureter. Wagner, referring to his clinical case, alluded to intra-ureteral hemorrhage following traumatism. Blood is allowed to remain, coagulate, and be organized because of ureteral paralysis and is, in our opinion, coincidental rather than causative in the development of hydronephrosis.

# STEWART AND BARBER

To study the physiological effect of such traumatism upon the ureter a dog was etherized to analgesia and the following observations made upon ureteral movements:

Case 160.—(1) Waves of ureteral peristalsis were noted at 9-second intervals. (2) Waves of ureteral peristalsis were noted at 16-second intervals with middle ureter stripped. (3) Waves of ureteral peristalsis were noted at 25-second intervals with greater part of ureter stripped. (4) Waves not continuous. Fibrillary contractions noted at 69-second intervals with ureter completely stripped. While at the same time waves of peristalsis were observed at 7-second intervals in normal ureter.

Case 161.—Case was similarly treated. Two ureters were exposed—one left intact, other stripped. On rolling normal ureter under finger contractions were elicited; on rolling stripped ureter under finger no contractions could be aroused.

From this observation it would appear that a cause of urinary stasis in the above experiments was ureteral paralysis. We, therefore, offer tentatively, and subject to further experimental proof as a cause of hydronephrosis, a ureteral condition analogous to adynamic ileus. It is true in several of the cases a mechanically obstructed ureter was found, but that such obstruction was irrelevant appears from a comparison of ten subsequent cases in which not one similarly obstructed ureter was found. These were cases in which the valve was cut and in addition, the ureter was stripped.

TABLE III  
SHOWING EFFECT OF STRIPPING URETER AND CUTTING URETEROVESICAL VALVE<sup>18</sup>

Case No.	Gross Findings	Microscopical Findings	Cause of Death	Days of Life
74	Normal	Normal	Hæmoperitoneum	0
80	Congested	Glomerular congestion	Hæmoperitoneum	2
72	Pyelonephritis	Suppurative nephritis; abscesses; suppurative ureteritis	Pyelonephritis	7
77	Pyelitis	Congested parenchymatous swelling	Pyelonephritis	3
73	Pyelonephritis	Suppurative nephritis	Pyelonephritis(?)	23
89	Congested kidney	Parenchymatous degeneration; congestion	Pyelonephritis	20
88	Parenchymatous degeneration	.....	.....	11
83	Pyelonephritis	Suppurative nephritis; abscesses; tubules distended with pus cells. Glomeruli free	Pyelonephritis	13
81	Pyelitis; congested kidney	Glomerular congestion	.....	18
84	Chronic nephritis	.....	Ether	121

Histologically, the various changes in the kidney in experimental hydronephrosis have not yet been studied in sufficient detail to warrant more than passing mention at the present moment. The first step, however, appears to consist of widespread intertubular and glomerular congestion followed by granular degeneration and hydropic changes in

## HYDRONEPHROSIS

the epithelium, particularly of the convoluted tubules. At a later stage, corresponding to moderately advanced dilatation of the pelvis, the cortical tubules become markedly distended, their lining epithelium undergoes atrophy and the interstitial tissues begin to show the effects of compression. Finally, with increasing dilatation of the pelvis and obliteration of the calyces, the kidney tissue becomes noticeably compressed and its individual elements—tubules and glomeruli—atrophy. In secondarily infected organs the mucosa of the pelvis is replaced by a thick membrane made up of degenerated polynuclear leucocytes.

Clinically, one of the recent cases occurring in the practice of one of the authors (Stewart) typifies the hydronephrosis complex and emphasizes the important relationship existing between experimental and applied surgery. In this case there were found at operation a large hydronephrotic kidney and a calculus snugly wedged into the ureteropelvic isthmus of the cephalad ureter. Through the courtesy of Professor Douglas Symmers, to whom we are indebted for the microscopical study of our specimens, it was determined beyond reasonable doubt that the specimen was an adult kidney which had undergone pressure atrophy from the extreme distention of the pelvis and calyces. Experimentally a similar case was produced in one of our dogs, dog No. 152, by a calculus accidentally slipped into the caudad ureter to the junction of the lower and middle thirds. But these cases, alike in their gross and microscopical pathology, corresponded with the specimens produced by paralyzing the ureters. There may be a relationship between the ureteral calculus and the prostatic wave that is in its effect the same as an atonic ureter. Especially does such a possibility seem likely when as in our human case the calculus intervened between the pelvic and straight portions of the ureter, the point where, as described by Lucas<sup>17</sup> and observed by us, a change occurs in ureteral contractions and functions.

### CONCLUSIONS

1. It is generally agreed that mechanical obstruction gives rise to urinary stasis and, when continued sufficiently long, to kidney distention.

2. This mechanical obstruction may be complete or incomplete, gradual or sudden. When the obstruction is sudden and complete transitory hydronephrosis with marked congestion follows. Atrophy intervenes and is proportionate to the duration of the obstruction.

3. Paralysis of the ureter is accompanied by urinary stasis and kidney distention in 66 per cent. of cases.

4. The pathological changes in hydronephrosis of functional origin correspond to the age of the adynamic ureter.

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- <sup>3</sup> Morris: *Surg. Dis. of the Kidney and Ureter*, vol. i, p. 395.
- <sup>4</sup> Rayer: *Maladie des Weins*, p. 476, vol. iii.
- <sup>5</sup> Bradford: "Observations Made Upon Dogs to Determine Whether Obstruction of the Ureter Would Cause Atrophy of the Kidney." *Brit. Med. Journal*, 1897, p. 1720.
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- <sup>7</sup> Chetwood: *Hydronephrosis: Its Etiology, Diagnosis and Treatment.* Am. Med., Burlington, Vt., and N. Y., 1912, N. P., vii, 97-104.
- <sup>8</sup> Delbet: "Hydronephrose partielle: contribution à la pathologie des Hydronephrose." *Ass. franc. d'ural. Proc.-verb. Par.*, 1911, xiv, 462-468.
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- <sup>13</sup> Cheput: *Arch. Gen. de Med.*, January, 1894, p. 5.
- <sup>14</sup> Zuerbelle: "Ueber Veränderungen und Untergang der Glomeruli bei Hydronephrose." *Frankfort, Ztschr. f. Path., Wiesb.*, 1912, x, 42-59, 3 pl.
- <sup>15</sup> Draper and Braasch: *The Function of the Ureterovesical Valve.* Reprint from A. M. A., presented at Atlantic City, 1912.
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- <sup>17</sup> Lucas: *Physiological and Pharmacological Studies of the Ureter.* III A. M. J. *Physiology*, vol. 22, July 1, 1908, No. 2.
- <sup>18</sup> Barber and Draper: *Renal Infection: A Further Experimental Study of Its Relation to Impaired Ureteric Function.*







## RENAL INFECTION

A FURTHER EXPERIMENTAL STUDY OF ITS RELATION  
TO IMPAIRED URETERIC FUNCTION \*

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Injuries, inflammation, neoplasms, and congenital defects of the ureter, urinary bladder, or associated organs could be more often successfully treated had we an effectual method of entero-ureteral transplantation. It is pointed out by Watson and Cunningham<sup>1</sup> after condemning all operations for diverting urine, with the single exception of Maydl's, that "the very large proportion of cases have proven fatal either as a result of the operation or because of the renal lesions which are produced later by ascending infection from the intestinal tract."

Eisendrath<sup>2</sup> holds that "reimplantation of the ureter into the lower bowel is impracticable on account of the irritant action of the urine on the mucous membrane, causing persistent diarrhea, and on account of the frequent occurrence of ascending infection." Carl Beck<sup>3</sup> adds "infection of the kidneys secondary to the operation and the difficult control of urination" as "principal drawbacks." In addition to ascending infection, colitis, difficult control of urination, shock, peritonitis following technical errors, may be mentioned to explain the general failure of entero-ureteroplasty. Maydl's block transplantation seems to have met with most success, since, as Cunningham<sup>1</sup> puts it, "ascend-

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\* Read before the Section on Genito-Urinary Diseases at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

1. Watson and Cunningham: Diseases and Surgery of the Genito-Urinary System, Chapter on Entero-Ureteral Anastomosis; Genito-Urinary Diseases, ii.

2. Eisendrath: THE JOURNAL A. M. A., Nov. 8, 1913, p. 1694.

3. Beck, Carl: Implantation of Ureter into Large Bowel, THE JOURNAL A. M. A., Nov. 8, 1913, p. 1691.



Fig. 1 (Dog 83).—Infection following cut valve and stripped ureter; external surface showing foci.

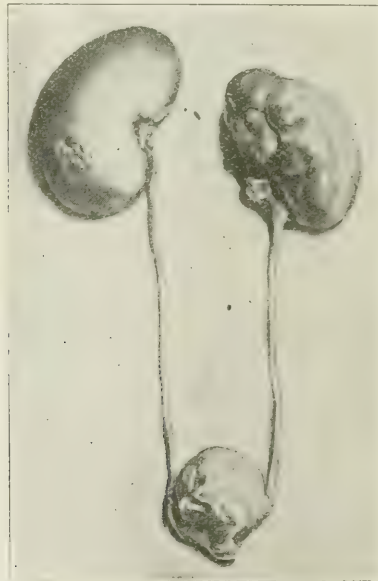


Fig. 2 (Dog 84).—Infection following cut valve and stripped ureter; typical of Series 3.

ing infection is less probable . . . because of the protection afforded by the preservation of the natural relations." It has been our object in this paper to study these "natural relations," define them, and estimate their respective values. It was hoped to gain information on which to found a more satisfactory technic



Fig. 3 (Dog 72).—Pyelonephritis.

for an entero-ureteral operation. Evidently it must be based on inductive knowledge of the obscure physiology of the ureter. Given the normal gross anatomic relations of kidney, ureter, and bladder intact, it is taught that renal infection may be urogenous.<sup>4</sup> Cases of probable ascending infection are reported

4. Blake, J. A.: Lectures Before Class in Surgery, 1910-11.



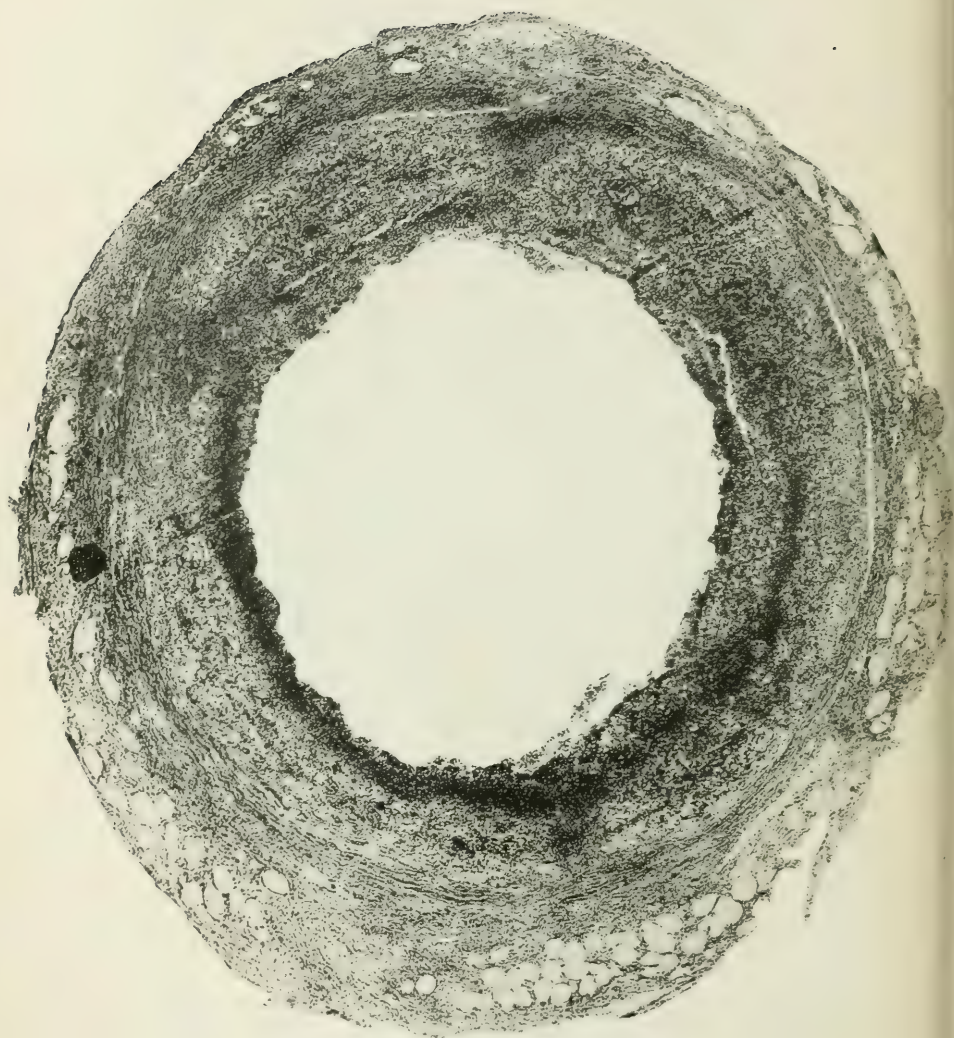


Fig. 4 (Dog 72).—Degeneration in wall of ureter.

clinically.<sup>5</sup> Individual opinion as to the occurrence or non-occurrence of "ascending infection" seems to be as diverse as the proven clinical cases are rare.

#### ESSENTIAL STATE OF BLADDER FOR ASCENDING INFECTION

Guyon and Albarran<sup>6</sup> pointed out that bacteriuria and retention were necessary for kidney infection.

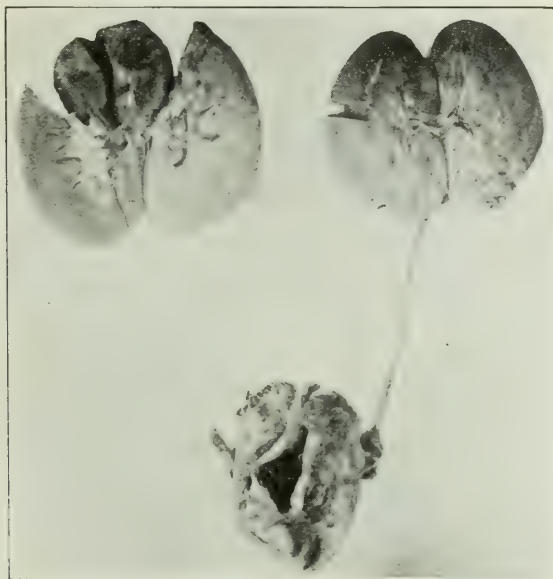


Fig. 5 (Dog 83).—Pyelonephritis following stripping ureter and cutting valve; cut surface (left) showing foci at cephalad pole.

Guyon<sup>7</sup> emphasized bladder sensibility and abnormal contractility with coincident cystitis. Courtade and Guyon<sup>8</sup> emphasized retention. Brewer<sup>9</sup> reviewed the

5. Le Brigand, Henri: Contribution à l'étude de la pyélonéphrite pendant la grossesse, Paris Thèses, 1899-1900.

6. Guyon, F., and Albarran, J.: Physiologie pathologique des rétention rénales, Tr. Assn. Franç. d'urolog., 1897 and 1898, ii, 11; Anatomie et physiologie pathologiques de la rétention d'urine, Arch. de méd. expér. et d'anat. path., 1890.

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8. Courtade, D., and Guyon, J. F.: Sur le reflux du contenu vésical dans les uretères, Compt. rend. Soc. de biol., 1894, x, Series 1, p. 556.

9. Brewer: The Present State of Our Knowledge of Acute Renal Affections, with a Report of Some Animal Experiments, THE JOURNAL A. M. A., July 15, 1911, p. 179.

work of these and other investigators and concluded the essentials to be (1) chronic cystitis; (2) acute retention with spasmodic contraction of the detrusor; (3) mechanical interference with ureteral sphincter. In our experiments we have not attempted to increase whatever retention may physiologically exist in dogs,



Fig. 6 (Dog 83).—Pyelonephritis.

although we realize that it may be important in the production of renal infection.

#### MECHANISM OF ASCENSION

It was held by Guyon<sup>7</sup> in 1890 that cystitis may give rise to ascending nephritis. It is interesting to com-

pare the findings of G. G. Smith's<sup>10</sup> analysis of ninety-eight cases of cystitis from the wards and the outpatient department of the Massachusetts General Hospital in which he pointed out that certainly not more than five had given rise to pyelitis by the ascending route, and that even this small number was doubtful. Renal infection from cystitis has been proved possible by different experimenters since, but the mechanism of its production is far from agreed on.



Fig. 7 (Dog 100).—Hydronephrosis following stripping of ureter.

Obviously, given a suppurating bladder, infection may ascend to the kidney outside the ureter through the ureter wall or through the lumen of the ureter. If it travels outside, it may follow the course demonstrated by Samson<sup>11</sup> and designated vesico-utero-ovario-renal anastomosis, and follow these blood vessels; or by the lymphatics, as demonstrated by Stew-

10. Smith, G. G.: Chronic Cystitis in Women Not a Disease, *THE JOURNAL A. M. A.*, Dec. 6, 1913.

11. Samson: Ascending Renal Infection, with Special Reference to the Reflux of Urine from the Bladder into the Ureter as an Etiological Factor in Its Causation and Maintenance, *Bull. Johns Hopkins Hosp.*, December, 1903, p. 334.



art<sup>12</sup> in eight out of ten transplanted dogs' ureters. The infection may ascend within the ureter wall apparently only under a pathologic condition of the ureter itself, such as shown by Samson's<sup>11</sup> clinical case of purulent cystitis, ureteritis with exudative swelling and occlusion of the ureter and suppurative

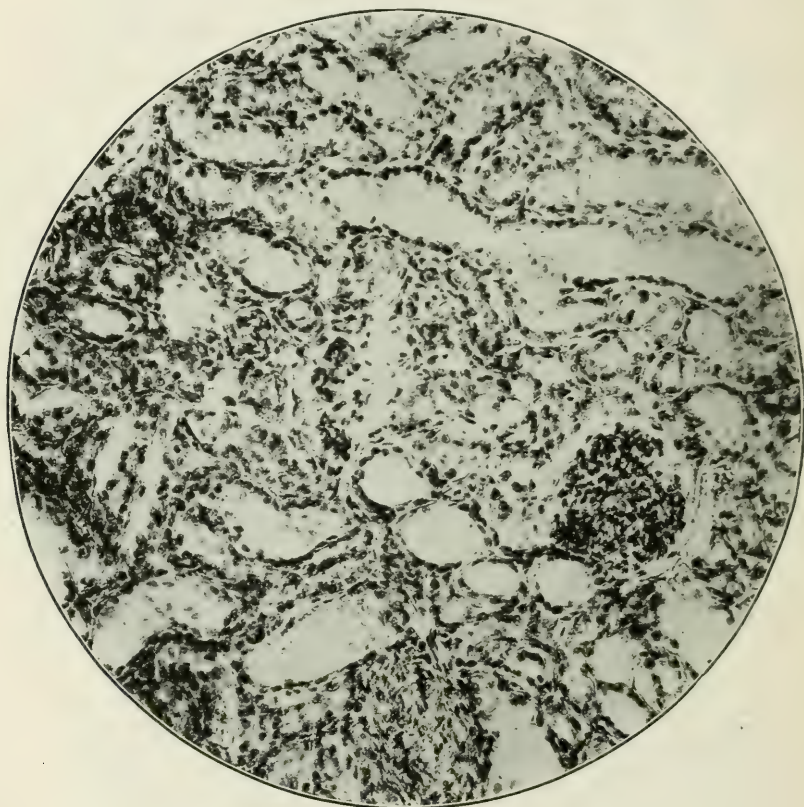


Fig. 8 (Dog 70).—Dilated renal tubules; hydronephrosis.

nephritis. If the infection ascends by the lumen of the ureter, several courses have been held by different investigators. It does not seem necessary to mention the method suggested by Kelly and repeated

12. Stewart, E. F.: A Study of Ascending Infection of the Kidney Carried Out by the Method of Transplanting the Ureter into the Intestines, Univ. Penn. Med. Bull., 1911, p. 233.



by Samson<sup>11</sup> of aspiration with air through the ureter during cystoscopy with the patient in the knee-chest position. Motility of the micro-organism is the means suggested by Guyon and Albarran,<sup>6</sup> on the basis of the difference in time of ascent between an inert colored particle and the colon bacillus; the ratio being roughly 2:1. If the organism

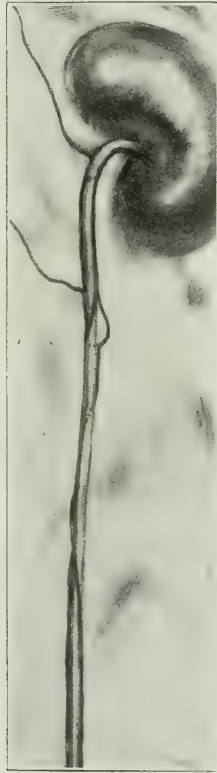


Fig. 9.—Semidiagrammatic drawings of some vascular relations of the upper ureter.

is a coccus and therefore immotile, it is thought to ascend partly by the processes of reproduction and extension along the ureteral wall, and partly by a to-and-fro motion of the ureter itself. Orth and Jacobelli supported Guyon and Albarran. Le Brigand<sup>5</sup> in 1900 concluded similarly from his clinical observa-

tions. This to-and-fro movement is qualified still further as "countercurrent" and "eddy" by Adjevoli.<sup>11</sup> C. J. Bond<sup>13</sup> experimenting with insoluble dyes described a mucous current in a partially collapsed ureter. Anastalsis and reflux complete the means of possible intra-ureteral ascension. Reflux has been described as occurring in rabbits by Lewin and Goldsmith, Courtade and Guyon,<sup>8</sup> Jacobelli, and Marcus.<sup>11</sup> Jacobelli maintains that the fluid must be injected suddenly<sup>14</sup> into the bladder for it to ascend the rabbit's ureter. Courtade and Guyon observed reflux in dogs. Marcus further showed reflux of urine in rabbits possible by anastalsis or vesical contraction when the ureters were distended. Disse<sup>11</sup> explained the patency of the ureteral valves under such circumstances by contraction of the longitudinal musculature of the ureter, thus converting it into an inflexible tube. On the other hand, Young<sup>15</sup> in several cases failed to get reflux in dog's ureter after injecting the bladder with colored solution. This agrees with the findings of Draper and Braasch.<sup>16</sup> Samson<sup>11</sup> tried out anastalsis and reflux in nineteen dogs. To each bladder was attached a normal ureter, a ureteral stump, and the reimplanted cut distal end. In no case having normal valve or with valve absent did he observe reversed ureteral current. But he held reflux possible in conjunction with diseased ureter. May it not be that the amount of injury to the ureter explains the varying results of these different investigators? We have distended the dog's bladder by a 4½-foot water column and noted no reflux in normal ureter with normal valve or in stripped ureter with normal valve. Suddenly injected fluid as observed by Jacobelli was noticed by us to collect slowly and drop from the cut end of stripped ureter with cut valve.

#### EMBRYOLOGY

It is known<sup>17</sup> that at the fourth week, the ureteric part of the kidney is apparent as a dilatation at the

13. Bond, C. J.: Ascending Currents in Mucous Canals and Gland Ducts and Their Influence on Infection: A Study in Surgical Pathology, Med. Rec., New York, Aug. 12, 1905.

14. Brewer's reference in THE JOURNAL A. M. A., July 15, 1911, p. 179: Sudden injection may temporarily paralyze the ureter.

15. Young, H. H.: Hydraulic Pressure in Genito-Urinary Practice, Especially in Contracture of the Bladder, Bull. Johns Hopkins Hosp., May, 1898, p. 100.

16. Draper, J. W., and Braasch, W. F.: The Function of the Uretro-vesical Valve, THE JOURNAL A. M. A., Jan. 4, 1913, p. 20.

17. Bailey: Text-Book of Histology, p. 208.

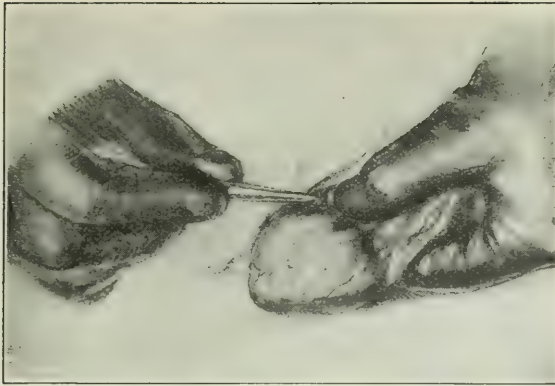


Fig. 10.—Technic of isolating and stripping ureter and irritating suppositional ureteral nerve plexus.

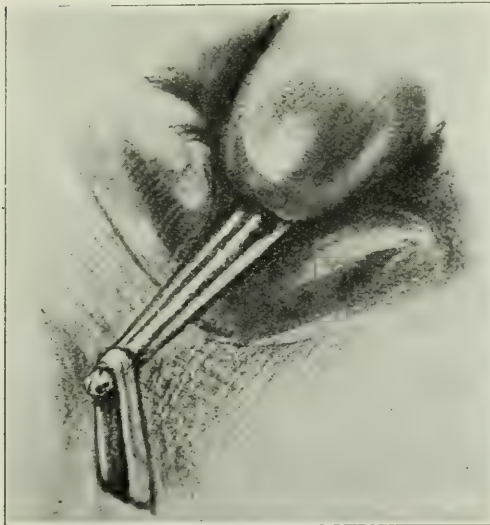


Fig. 11.—Technic of isolating and stripping ureter and irritating the suppositional ureteral nerve plexus.

caudad end of the wolffian duct, near the cloaca; the nephritic tissue being represented in the sacral region. At the beginning of the second month the ureteric bud grows out against the nephritic tissue in the sacral region. By the end of the second month the renal bud has ascended to the lower part of the lumbar region, passing dorsad to the wolffian body; the ureter and its pelvic calyces can now be recognized. When we consider mammalian embryology and the close relationship of birds with their permanent cloacal arrangement to the mammals, there appears a phylogenetic as well as an ontogenetic basis for believing that the human body should be capable of assuming vicariously the recently lost function of storing urine. Furthermore, Huntington<sup>18</sup> calls attention to the origin of the bladder from the cloacal or intestinal space and to the relationship as shown in one of our larger American lizards, *Igriana tuberculata*, between the adult reptile and certain stages in the development of the mammals respecting the common termination of the genito-urinary and intestinal tracts.

#### ANATOMY

Anatomically the ureter is of course well understood. The vesical end is reinforced by a fibrous sheath which envelops the ureterovesical junction. The ureteral musculature is replaced as it reaches the vesical submucosa by longitudinal fibers arising from the bladder and paralleling the ureter within the bladder wall. The ureteral mucosa blends with that of the bladder, forming the orifice of the ureterovesical valve. The ureter is enclosed throughout in peritoneum, beneath which it derives blood, lymph and nerve supply. The blood supply has been mentioned. The lymphatics have been carefully worked out by Sakota. The nerves of the ureter are derived from the sympathetic.

#### PHYSIOLOGY

Physiologically much less is known. In speaking of the nerve control of the ureter Lucas<sup>19</sup> says:

I believe that further research will justify the general division of the ureter into the following two portions: 1. The

18. Huntington: Genetic Interpretation of Some Variations of Genito-Urinary Tract, Harvey Lectures, Series 2, 1906.

19. Lucas: Physiological and Pharmacological Studies of the Ureter, Series 3, Am. Jour. Physiol., July 1, 1908.

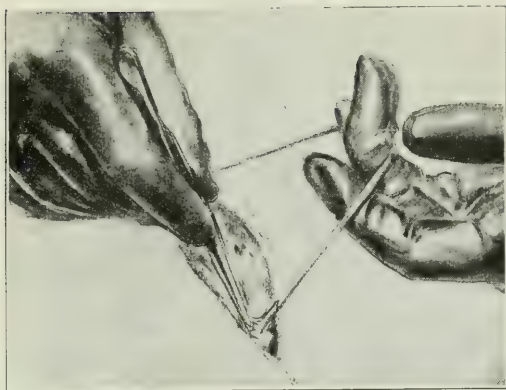


Fig. 12.—Technic of isolating and stripping ureter and irritating the suppositional ureteral nerve plexus.



Fig. 13.—Technic of Series 4; circumcising vesical end of ureter.



funnel-shaped portion cephalad to the isthmus contained in the renal pelvis and probably partaking of the nerve distribution of the kidney. 2. The straight portion extending from the isthmus to the bladder, which may be subdivided into (a) a cephalad third, containing nerve endings in its wall; (b) a middle third deficient in nerve endings, and (c) a caudad third, adjacent to the bladder and partaking to some extent in the nerve distribution of the bladder.

Von Bardeleben<sup>20</sup> holds that the renal plexus supplies the pelvis and the cephalad half of the abdominal part: the spermatic, the caudad half of the abdominal part; and the hypogastric, the pelvic portion. Ganglia and nerve ends he found in adventitia, large at the ends and small in the middle of the ureter. Piersol<sup>21</sup> and Cunningham support Bardeleben.

It is evident that the origin of muscular contractions of the ureter, whether neurogenic or myogenic is not understood, but that it is a matter of observation that rhythmical contractions do exist. They occur in peristaltic waves, which, beginning with the kidney pelvis, progress toward the bladder at average intervals of 9 seconds in the dog, according to our own observations. Urine appears to be forced into the bladder by each peristaltic contraction. These contractions appear to be quite persistent as long as the normal relations of the ureter are preserved, but variable in force and frequency when these are disturbed. Moreover, this irregularity in ureteral peristalsis seems to vary in direct proportion to the degree of trauma to the organ. We believe that a complete removal of the ureter from its retroperitoneal bed affords a valuable technical index for the experimental study of renal lesions. It has evidently entered as an unobserved and uninterpreted complex into much of the clinical and experimental study reported to date without having been given due consideration as a causative factor. In brief, ureteral dislodgment causes a condition roughly analogous to so-called "adynamic ileus" of the gut.

#### EXPERIMENTAL PROCEDURE

We present for consideration the following proposition: Given a foreign body cystitis the local factors determining infection are:

20. Von Bardeleben: *Handbuch der Anatomie des Menschen*, vii, Part 1, p. 112.

21. Piersol: *Human Anatomy*, p. 1898; *Normal Histology*, p. 201.



Fig. 14.—Technic of further step in circumcising ureter.



Fig. 15.—Technic of completed step in circumcising ureter.

1. The ureterovesical valves, and
2. The peristalsis of the ureter.

These factors may be made experimental variants as follows:

- By 1. Cutting of the valve.
2. Disturbance of ureteral peristalsis.
3. Combination of 1 and 2.
4. Ureteral circumcision.
5. Combination of 2 and 4.
6. Combination of 1 and 4.
7. Combination of 1, 2 and 4.

These may be considered in detail as regards experimental findings.

Our experiments have been made on dogs, forty in all having been used exclusive of Draper-Braasch series. Each

TABLE 1.—EFFECT OF STRIPPING URETER AND CUTTING VALVE \*

RENAL INFECTION

Case No.	Gross Findings	Microscopic Findings	Cause of Death	Days of Life
74	Normal	Normal	Hemoperitoneum	0
80	Congest.	Glom. congest.	Hemoperitoneum	2
72	Pyelonephritis	Sup. nephritis; abscesses; sup. ureteritis	Pyelonephritis	7
77	Pyelitis	Cong. parenchym. swelling	Pyelonephritis	3
73	Pyelonephritis	Sup. nephritis	Pyelonephritis	23
89	Congested kidney	Parenchym. degeneration; congestion	.....	20
88	Parenchym. degeneration	Parenchym. degeneration; hydropic degeneration; pronounced	Parenchym. degen.	11
83	Pyelonephritis	Sup. nephritis; abscesses; tubules distended with pus cells; glom. free	.....	13
81	Pyelitis; congested kidney	Glom. congest.	.....	18
84	Chr. nephritis	.....	Ether	121

\* This and following tables represent work done at the Experimental Surgical Laboratory, New York University, 1913-14.

dog had received a maximum dose of morphin sulphate per kilo of body-weight, followed by profound ether anesthesia. Each case was subsequently nephrotomized, and an appropriate section preserved for a microscopical index of normal kidney.

TABLE 2.—EFFECT OF STRIPPING URETER

## RENAL INFECTION

Dog No.	Gross Findings	Microscopic Findings	Cause of Death	Condition of Ureter	Bacterial Findings	Days of Life
103	Hydronephrosis	Congestion Dilated tubules Dilated tubules	Intussusception Hydronephrosis Hydronephrosis	Patent Stenosed Patent	Coccus colon-like organism Coccus colon-like organism No change in fixation test for colon	7
70	Hydronephrosis					21
17	Hydronephrosis					.....
54	Hydronephrosis; hydronephrotic pyonephrosis	Nephritis Purulent nephritis Glomerular congestion	Hydronephrosis Pyonephrosis Perforation of bladder	Patent Stenosed Patent	Culture omitted Coccus colon-like organism No change in fixation test for colon	25
69	Pyonephrosis					29
21	Normal					24
22	Parenchymatous	Parenchymatous	Peritonitis (technical)	Patent	No change in fixation test for colon	8
24	Interstitial nephritis	Productive nephritis	Pneumonia	Patent	Culture omitted	121
100	Hydronephrosis	Nephritis	Hydronephrosis	Stenosed	Culture omitted	69

TABLE 3.—EFFECT OF CIRCUMCISING URETER

RENAL INFECTION				
Dog No.	Gross Findings	Microscopic Findings	Cause of Death	Days of Life
110	Normal	Hemorrhagic kidney; congest. glomeruli	.....	5
112	.....	.....	Anesthetic Leakage	0
91	Normal	.....	Peritonitis following perforation of bladder	0
109	Normal	Normal; congest glomeruli	Leakage	12
117	Normal	Only one kidney was found at operation. Other kidney had been replaced by a parasitic cyst. Parasite was later identified as <i>Dis-tophyme renal</i>	.....	60
106	Normal	Normal	Pneumonia	60
92	Normal	Normal or moderately congested	Shock	1½

TABLE 4.—EFFECT OF CIRCUMCISING AND STRIPPING OF URETER

RENAL INFECTION				
Dog No.	Gross Findings	Microscopic Findings	Cause of Death	Days of Life
129	Pyonephrosis	Purulent nephritis	Pyonephrosis	29
*131	Hydronephrosis; hydro-ureter	Parenchym. degeneration very marked with conv. tubules crowded with granular casts; glomerular congest.	Hydronephrosis	6
68	Normal	Coagulated albuminous, exudate in Bowman's caps.	Leakage	2

\* Colon bacillus was identified in both left and right kidneys. The presence of this organism in both kidneys was probably due to post-mortem invasion.

TABLE 5.—EFFECT OF CIRCUMCISING URETER AND CUTTING VALVE

RENAL INFECTION				
Dog No.	Gross Findings	Microscopic Findings	Cause of Death	Days of Life
*122	Hydronephrosis; hydro-ureter	Glomerular and intertubular congestion; cloudy swelling; parenchymatous degeneration.	Leakage	2
123	.....	.....	Anesthetic	0
113	Normal	Glomerular congest.; cloudy swelling	Infectious skin disease	50

\* Ureter was found adherent to circularly incised wound of bladder 1 cm. distant from ureterovesical junction. This accounted for condition of kidney and ureter.



TABLE 6.—EFFECT OF CIRCUMCISING AND STRIPPING URETER AND CUTTING VALVE

RENAL INFECTION				
Dog No.	Gross Findings	Microscopic Findings	Cause of Death	Days of Life
*139	Normal	Congestion; bacteria in kidney	.....	3
*151	Normal	.....	Leakage	1
153	Normal	.....	.....	18
152	Hydronephrosis following ureteral calculus Enlarged; lobulated; tense. Contained 80 c.c. clear fluid Paren.—shell Cal.—dilated Pus.—none	Typical hydronephrosis; compression and atrophy of tubules and glom.; moderate cellularity and plus conn. tissue	Euthanasia; great emaciation	57

\* The streptococcus and colon bacillus were found in both kidneys of No. 139. Streptococcus was found in left kidney of No. 151. No bacteriologic examination of right kidney of No. 151 was made. The presence of these organisms appeared to be due to post-mortem invasion.

1. *Cutting of the Uretrovvesical Valve.*—See Draper-Braasch series. A further technical point in valve cutting that seems worthy of note is that in attempting to cut the valve either do not traumatize the valve area at all, which ensures the natural color relations, or traumatize severely, which converts the valvular orifice into an ischemic ring.

Result (10 cases): No substantial kidney change.

2. *Disturbance of Ureteral Peristalsis.*—In nine cases the ureter was removed from its retroperitoneal bed, stripped of every recognizable vessel, nerve and fascial connection from kidney pelvis to bladder insertion. In order to make sure that it was absolutely freed from all nervovascular connections throughout its course, as well as to disturb the nerve plexus in the adventitia of the ureter, the ureter was rubbed snugly with dry gauze throughout. It was then allowed to drop back into the peritoneal cavity.

In each case of these series a cubical foreign body infected with autogenous colon bacilli and other organisms, and of such shape as not to cause valvular ureteral obstruction, as suggested by Draper and Braasch, was placed in the bladder through a mesoventrad incision so that, as subsequent examinations of urine and bladder revealed, a purulent cystitis was produced.

Result (9 cases):<sup>22</sup> Hydronephrosis in various stages.

3. *Combination of 1 and 2.*—Result (10 cases): Pyelonephritis may follow. But the lower segment of straight portion of the ureter is supplied by the sympathetic through the vesical plexus. To eliminate a possible nerve control through such recurrent fibers the following observations were made by

<sup>22</sup> Barber, Stuart and Symmers: Hydronephrosis: An Experimental Study.

4. *Ureteral Circumcision*.—In circumcising the valve an incision was carried about the ureterovesical implantation through the serosa, muscularis and submucosa to the firm, comparatively resisting, vesical mucosa. When completed this incision was carefully closed by continuous suture.

Result (7 cases): No kidney change.

5. *Combination of 2 and 4*.—Result (3 cases): Hydro-nephrosis.

6. *Combination of 1 and 2*.—Result (3 cases): No kidney change.

7. *Combination of 1, 2 and 4*.—Result (4 cases): No kidney change.

Therefore the severing of whatever nerve supply enters the ureter from the bladder appears to play no essential part in the possible renal infection.

#### CONCLUSIONS

Given an infected bladder and making due allowance for systemic and local resistance:

1. The ureterovesical valves can be cut without resulting renal infection. Duration of life indefinite.

2. If the ureter is circumcised to but not through the vesical mucosa the kidney remains normal. Duration of life indefinite.

3. Ureteral traumatism resulting in greater or lesser degrees of impairment of function as indicated by prostatic paralysis, resulted in 75 per cent. of cases in hydronephrosis which in the early stages were not infected: a mechanically changed kidney which might or might not be infected later. Average duration of life, 30.33 days.

4. If the valves were cut and the ureters were paralyzed, hydronephrosis did not occur, but the kidneys underwent a primary infective change in 50 per cent. of cases. Average duration of life, 13.57 days.

At the beginning of this paper it was stated that our object was to study, define and estimate the respective values of the "natural relations" of the ureter.

The integrity of the "factor of safety" which protects the kidneys both from urogenous infection and from hydropic degeneration appears to depend directly on the unimpaired prostatics of the ureter; indirectly on the integrity of the ureterovesical valve and most interestingly on the relationship between these physiologic and anatomic barriers.

The authors acknowledge the constructive criticism of Prof. George D. Stuart and Prof. Douglas Symmers; also the detailed assistance of Dr. A. G. Bennett and Dr. W. C. Noble of the department of bacteriology.

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**URETERO-ENTERIC ANASTOMOSIS**

A NEW ENTERO-URETERAL OPERATION  
AN INDUCTIVE STUDY BASED ON SURGICAL PHYSIOLOGY

BY W. HOWARD BARBER, M.D.  
OF NEW YORK

(From the Laboratory of Experimental Surgical Physiology, N. Y. University)

THE ureterovesical valves may be destroyed without resultant injury to the kidney tissue. This was amply shown by Draper and Braasch<sup>1</sup> at the Mayo Clinic in 1911.

The causative factors of ascending infection were further studied by Barber and Draper<sup>2</sup> and Stewart and Barber<sup>3</sup> in 1913-1914. From a study of 42 dogs it was determined that:

(1) When the ureters were "stripped" hydronephrosis followed in 75 per cent. of the cases.

(2) When the ureters were "stripped" and the valves were cut, renal infection ascending through the wall or the lumen of the ureter or both followed in 50 per cent. of cases.

(3) When the ureteral vesical implantations were circumcised no kidney changes were observed.

From a review of these conclusions it appeared that:

(1) If the ureters were transplanted without traumatization, preserving the ureterovesical valve or its equivalent was desirable.

(2) If the ureters were traumatized in attempting transplantation, the absence of a ureterovesical valve or its equivalent was desirable.

(3) And in either case transplantation of the ureter was in itself no causative factor, but a protective factor against ascending lymphatic infection.

The problems of the anastomosis of the ureters and the intestine have been shock, peritonitis, cumbersome technic, difficult control of urination, colitis, leakage, hydronephrosis, and primary infective kidney. To these should be added and emphasized, the inevitable dis-

<sup>1</sup> Draper and Braasch: The Function of the Ureterovesical Valve. *Journal A. M. A.*, 1913.

<sup>2</sup> Barber and Draper: Renal Infection; A Further Experimental Study of its Relations to Impaired Ureteric Function. *Journal A. M. A.*, 1914.

<sup>3</sup> Stewart and Barber: Hydronephrosis; an Experimental Study. *ANN. SURG.*, December, 1914.

quietude of the surgeon arising from his ignorance of the intra-ureteral pressure.

From a review of these conclusions it appeared that:

(1) An operation removing the elements of shock, peritonitis and cumbersome technic must be brief, clean, and simple.

(2) An operation removing the objectionable factor of difficult control of urination must result in normal sphincteric control.

(3) An operation removing the occurrence of colitis must involve a mucous surface accustomed to or adaptable to contact with urine.

(4) An operation to prevent leakage and allow cognizance of either the patency or stenosis of the ureter must have an effectual anastomosis and one open to investigation at any time.

(5) Finally, a technic preventing post-operative hydronephrosis and primary infective kidney, if available, is to be found not by hit or miss methods based on anatomical findings, but only through the application of the recently acquired physiological knowledge of the ureter and kidney.

The following operation is not recommended to clinicians for trial at the present writing. Its interest primarily lies in its being the logical sequence of physiological laboratory facts, applied to the recognized problems, incident to the uretero-enteric anastomosis. Of eight dogs so operated upon all survived operation, one alone died within the first week, following sloughing of the ureter from overtension. The others to all appearances resemble normal dogs. It is expected that the following technic shall remove the objections common to other operations and leave but one serious problem for consideration; namely, that of the balance of power and load perttainable to every transposed ureter. For the ureter is necessarily traumatized and reduced in its motor efficiency and resistance is unavoidably piled up at its extreme caudad end. The problem, then, is simply so to reduce this terminal work that the already impaired ureter may physiologically meet it. The following technic is therefore proposed: A mesoventrad incision 5 cm. long is made in lower abdomen. Identify the ureter and free it from its bed. Divide the ureter between two ligatures just cephalad to the bladder. Attach a straight cutting needle to the cephalad ligature and penetrate the sigmoid colon in a line perpendicular to its long axis. Drive the needle through at a point 90 degrees distant on intestinal wall, thus drawing ureter through each wall. The sigmoid is then suspended within the wound by the usual glass rod method. The ligated cephalad end of the ureter is allowed to protrude on to the skin where its liga-

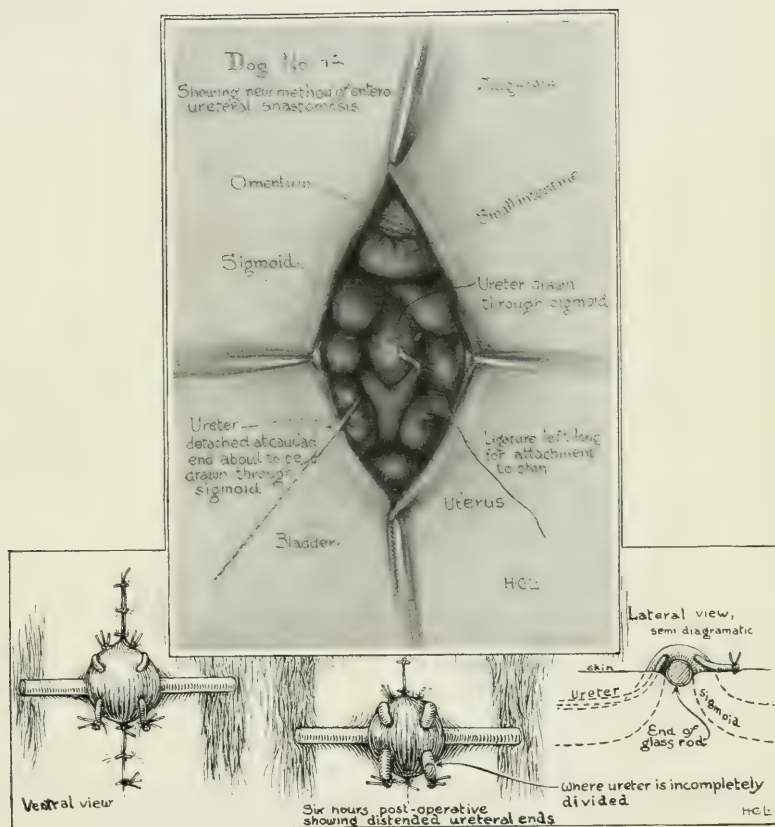


FIG. 1.—Technic of ureterosigmoid transplantation.





## URETERO-ENTERIC ANASTOMOSIS

ture is fixed by a single suture. The wound is then closed about the sigmoid and the ureter. Six hours later the exposed ureter is incompletely cut and allowed to empty. It may be returned to the lumen of the intestine at any time thereafter, but it is well to retain it under control until its continued patency is assured. One or both ureters may be transplanted in this way within twenty minutes. An exposition of the rationale and an interpretation of the results of the operation is forthcoming.





91 (1023)

Notes on the surgical physiology of the dog.

By W. HOWARD BARBER and JOHN W. DRAPER.

[From the Laboratory of Experimental Surgery, N. Y. University.]

I. HYDRONEPHROSIS AND HYDROURETER.

In a previous communication<sup>1</sup> the possible causal relationship of a paralyzed ureter to dilatations of the ureter and kidney pelvis has been pointed out. Of the experiments performed in 1913, 75 per cent. showed hydronephrosis in some degree. Last fall the same technic was repeated in twelve dogs with the following results:

- 2 Negative.
- 6 Hydronephrosis—to some degree.
- 1 Hydroureter.
- 3 Dilatation of cephalad ureter.

Therefore fifty per cent. showed hydronephrotic change and eighty-three and one-third per cent. hydronephrotic and hydroureteric changes combined.

It was realized in applying this information to the origination of a physiological uretero-sigmoid union, some traumatization of the transposed ureter and therefore some impairment of ureteric function was absolutely unavoidable. But making allowance for this reduced prostatic power by the least possible *total* ureteral traumatization and by purposely confining the necessary handling to the negligible caudad third, an effort has been made to balance such impaired power by a physiologic load. To this end twenty dogs have been operated upon by transplanting one ureter in seven and both ureters in thirteen dogs. The results were as follows:

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<sup>1</sup> Stewart and Barber, Hydronephrosis, *Annals of Surgery*, Dec., 1914, Barber and Draper, Renal infection, *Jour. Amer. Med. Assoc.*, Jan., 1915.



1. Direct uretero-sigmoidal entrance was found more obstructive than the oblique entrance.

2. When ureteral dilatation occurred it appeared first in the cephalad third of the ureter. This was associated in the animals having greater caudad obstruction with dilatation of the second or second and caudad thirds of the ureter and renal pelvis.

3. Each of the seven dogs with singly transplanted ureters showed hydronephrosis in some degree. The ureter in each case had been made to enter the sigmoid directly or obliquely for not over 0.5 cm.

4. Of the thirteen with doubly transplanted ureters, three showed cephalad ureteral dilatation only. These were dogs in which the ureters traversed the sigmoidal wall for 1.5 cm. The thirteenth dog with an intramural ureteral segment of 2 cm. on one side and a direct entrance on the opposing side after seventeen days of life, showed a normal kidney and ureter on the oblique and a pyonephrosis on the direct side.

## 2. ENTERIC DILATATION.

### A. *Small Intestine.*

Fourteen animals have been incompletely obstructed about the ileocecal region to determine a possible dynamic change in the cephalad end of the small intestine. The conclusions have been these:

1. A fixed diameter of the caudad ileum of approximately 1 cm. (incomplete obstruction) is followed in 5.8 days by a dilatation of a duodenum of mean volume of 12.2 c.c. to a mean volume of 19.2 c.c.

2. A fixed caudad ileac diameter of 0 (complete obstruction) is followed by a contraction of a mean duodenum of 14 c.c. to a mean of 6.25 c.c. in five days. A similar result was noted after acute gangrenous typhlitis and incomplete obstruction of the cephalad colon.

### B. *Colon.*

Six experiments have been performed on the colon. Incomplete obstruction of the extreme caudad colon for a mean of 10.75 days was followed by a dilatation of a cecum of a mean volume of 18 c.c. to a cecum of 29.5 c.c.



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**THE NATURE OF SHOCK.**

ITS RELATION TO ACAPNIA AND TO CHANGES IN THE CIRCULATION OF THE  
BLOOD AND TO EXHAUSTION OF THE NERVE CENTRES.\*

(From the Laboratories of Physiology and Experimental Surgery of the  
University and Bellevue Hospital Medical College.)

BY HENRY H. JANEWAY, M.D.,

AND

EPHRAIM M. EWING, Sc.D.,

OF NEW YORK.

It is the object of this paper to present the results of a series of experiments which furnish information regarding the relative etiologic importance of acapnia, of reflex changes in the circulation of the blood and of exhaustion of the nerve centres in shock produced by three methods. Crile has concluded as a result of a long series of experiments that the primary change wrought by all causes of shock is a fatigue of the vasomotor centre. As a consequence of this fatigue there is a continuous lowering of the blood-pressure until the cerebral centres, particularly the medullary centres, no longer receive sufficient blood to enable them to functionate normally, and from this cause, in fatal cases, life becomes extinct.

This theory has received the recognition to which it is entitled by the high character of all the work of its chief advocate. The protocols of his experiment demonstrate the close relation between low blood-pressure and shock. At present the theory is made the basis of a method of anæsthesia which is believed to diminish shock in operations, and is rendered conspicuous by having been christened with a new name.

No one can fail to admit the important association of a diminution of blood-pressure with the onset and development

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\* Read in the Section on Pathology and Physiology of the American Medical Association, at the Sixty-fourth Annual Session, held at Minneapolis, June, 1913.

of shock. Every writer has felt obliged to admit its bearing on the problem of shock. Nevertheless, a rather large number of writers since the publication of Crile's work have been unable to believe that any of the series of events, including the low blood-pressure itself, which may result in shock is, at the start, a process of fatigue of the nerve centres. Meltzer has discussed the whole question at length in a review of all the more recent theories of the nature of shock. He presents many observations of others and adds the results of his own experiments to show that the primary changes in the human body leading to the development of shock is not fatigue of the nerve centres but an inhibition of their activities. Differing from Crile, he quite justly questions the legitimacy of distinguishing etiologically between shock and collapse.

During the past winter we have performed experiments in connection with the production of shock by three methods. These experiments in agreement with the views of others, particularly of Howell, Porter and Meltzer, demonstrate, first, that a low blood-pressure is an important symptom of shock, but that an animal may pass into shock with a blood-pressure which is still far above a point below which the nervous system fails to functionate normally; and, second, that changes in the frequency of the heart and its output per beat always accompany shock, even in the earliest stages; but that it is very unlikely that changes either in the blood-pressure or in the force and output per beat of the heart are inaugurated by fatigue of the nerve centres. Our experiments indicate that shock in its incipency in some cases is of reflex, and in other cases of local peripheral origin.

From the practical as well as the scientific point of view the causes inaugurating shock are the most important. It matters little that a low blood-pressure may cause the death of an animal already in fatal shock. We wish to know what are the causes leading to shock before the blood-pressure begins to fall, and how to prevent these causes from becoming active.

Yandell Henderson has sought an explanation different from that of all other writers. He concludes from a large

amount of experimental work that acapnia can be one of these causes. He believes it to be the essential cause in shock produced by artificial hyperrespiration and by prolonged exposure of the intestines, and may be a cause of that form of shock produced by severe stimulation of afferent sensory nerves.

In all experiments performed by us, dogs were used. Each animal received 0.005 mg. of morphin for each kilogram of body-weight. Sufficient ether was given during each experiment to produce full anæsthesia.

#### SHOCK AND ARTIFICIAL HYPERRESPIRATION.

In the first series of experiments that form of shock was considered which was produced by artificial hyperrespiration.

A suitable time after the injection of the morphin the animal was etherized and a rubber tube introduced through the larynx into the trachea. By means of two rotary blowers and an intervening slide-valve which regularly threw first the exhaust of one blower and then the intake of the other blower into connection with the intratracheal tube, air was alternately forced into and sucked out of the lungs. The slide-valve was operated by another electric motor than either of those turning the blowers. Its speed was regular and could be controlled by a rheostat, and the frequency of the interruption of the valve which it operated could be varied as occasion demanded. By means of by-passes in series with the exhaust of the blower used to inflate the lungs, and the intake of the blower used to deflate the lungs, the amount of air used for the artificial inspiration and expiration could be varied at will. In these experiments the intratracheal catheter did not tightly fit the trachea. Provision, therefore, was made for the escape of any excess of air forced into the lungs during the inspiratory phase around the intratracheal tube, and the same factor of safety controlled the expiratory phase. We found, without this provision for a certain latitude in the amount of air used to inflate and deflate the lungs, that sudden death from excessive variations of pressure within the chest could occur. As will be developed, this fact is in accord with our own belief as to the cause of shock produced by excessive artificial respiration.

In four of these experiments which we have performed, the artificial respiration varied from 60 to 70 times a minute, and the lungs were as completely inflated and deflated as is possible with a closed chest. In order to accomplish such a filling and emptying of the lungs at a rate of from 60 to 70 times a minute, the air must be forced into and sucked out of the trachea under considerable pressure. Two of the experiments were continued for three hours and two for two hours. In these experiments the blood-pressure fell 40 per cent. within a few minutes after starting



the artificial respiration and then decreased more slowly to between 40 and 50 mm. of mercury. After the cessation of the experiments, the blood-pressure rose from 60 to 90 per cent. within a few seconds.

The carbon dioxide content of the arterial blood at the end of the experiments was from 38 to 44 per cent. of its original amount. The amounts of carbon dioxide and oxygen were measured in all experiments reported in this paper by the Barcroft-Haldane method. At the end of the experiment the animals were in deep shock. One died the next morning, one in two days and the other two lived three days. None of them died of the immediate effects of the experiment, but from secondary effects. They had recovered from the shock and their lungs at necropsy showed interstitial emphysema. In all these experiments it was found that the amplitude of the pulse and the blood-pressure was proportional to the pressure at which the lungs were inflated and, therefore, to the intrathoracic air-pressure. The amount of shock which was produced was proportional to the length of time that certain pressures, which we may term critical intrathoracic pressures, were maintained. The carbon dioxide content of the arterial blood could be easily reduced to from 40 to 50 per cent. of its original amount within half an hour; but in four other experiments when artificial respiration was maintained for only this short period, we found that no shock resulted. It has been assumed by Henderson that a long-continued acapnia, lasting two to three hours, results in a depletion of the tissues' store of carbon dioxide by osmosis, and accompanying this osmosis of carbon dioxide from the tissues into the blood, water passes from the blood into the tissues. As a consequence, a diminution of the total volume of the blood ensues. The associated general muscular relaxation dependent on the changed chemical composition of the muscles contributes to the diminution of the general blood-pressure by no longer affording the proper support to the veins. Thus the venopressor mechanism is also disturbed and, with it, the proper balance of the distribution of the blood in the body.

In our experiments the force of the artificial respiration necessary to produce acapnia was so excessive and the degree of shock and the change of blood-pressure so closely proportional to the intratracheal pressure that the air-pressures, at which the artificial respiration was given, seemed to us to be the most important factor in the production of shock by this means. We therefore performed three experiments in which the same conditions of artificial respiration were maintained, but with the provision against the loss of carbon dioxide. In all three precisely the same conditions of artificial respiration were maintained as in the first set of experiments, but, by inserting a rebreathing bag in which the expired air was collected and from which that blower was supplied which furnished the

air to the dog's lungs, and supplying to the fresh air required to be added during the experiment a proper proportion of carbon dioxide from a tank, the amount of oxygen in the blood was unchanged at the end of the experiment and the amount of carbon dioxide raised only slightly above the normal. All of these animals presented the same degree of shock at the end of their period of artificial respiration (two hours) as the animals of the first series. In these experiments, also, the shock was directly proportional to the air-pressures used during the artificial respiration.

Clearly, then, the shock produced by artificial hyperrespiration was not due to a diminution of carbon dioxide but to some other factor which is dependent on increased intrathoracic pressure. Of the effects produced by increased intrathoracic pressure, the one first suggesting itself as the most important and, as far as we can conceive, the only one bearing on the problem of the cause of this form of shock, is the interference of the venous return to the heart. By venous return to the heart, not only the return from the systemic circulation is referred to, but also the return from the pulmonary veins. The latter is affected in two ways, first, by direct pressure around the pulmonary artery, and second, on capillaries and veins within the lungs themselves. The pressure on the pericardium required to alter the general blood-pressure is much above that which affects the circulation when applied to the great veins at the base of the heart. This factor, therefore, can be neglected in these experiments. The most direct manner of measuring the effects of increased intrathoracic pressure on the circulation is to measure the output of the heart; and a third series of experiments, four in number, were devoted to this investigation.

The thorax was opened laterally, and a T-tube connected with a water manometer was tied in a small bronchus. The heart was then enclosed in a Henderson's cardiometer in circuit with a recording tambour. The blood-pressure was recorded from the carotid artery. The thorax was then closed and the animal subjected to intratracheal insufflation from an apparatus provided with an exhaust-valve which reduced the pressure to approximately zero from four to twelve times a minute, or

could be made to furnish continuous insufflation. In one experiment taken as an example, with an increase of intrabronchial pressure from 8 to 30 mm. Hg, the blood-pressure sank from 122 to 55 mm. Hg and the volumetric tracings of the cardiometer showed a diminution of cardiac output of 44 per cent. In another experiment the blood-pressure rose 15 mm. Hg each time the interrupting valve reduced the intrabronchial pressure from 6 mm. to 0. These variations of blood-pressure were completed within a few seconds after the change in intrabronchial pressure and could be duplicated at will. A rise of intrabronchial pressure above 8 or 10 mm. Hg always caused a fall of blood-pressure proportional to the rise of intrabronchial pressure.

It is evident, therefore, that excessive intrabronchial pressure, such as always accompanies violent artificial respiration even at from sixty to seventy times a minute, is quite sufficient in itself to account for a continued diminished cardiac output and low blood-pressure.

#### VENTILATION OF THE ABDOMINAL CAVITY.

We next studied the relation of acapnia to that form of shock produced first by exposure of the intestines to a current of warm moistened air passed over them beneath a celluloid cover, and second, by evisceration and handling the intestines.

A portion of the anterior musculature of the abdomen was excised, the omentum cut away and a celluloid window fitted in place between the layers of the muscles left at the side in such a manner as to completely cover the intestines. A current of warm and moistened air was then passed beneath the celluloid over the covered intestines. The air entered through a tube piercing the celluloid at one end of the abdomen and passed out through an opening at the other end. Aëration of the abdominal cavity under these conditions for a period of three hours produced no shock in one experiment and little reduction of the carbon dioxide content of the blood. Through the celluloid it could be seen that no drying of the peritoneal surface occurred. The intestine remained a good color, and peristalsis was almost absent at the end of this time. The blood-pressure was 163 mm. Hg. The celluloid membrane was then removed, the intestines spread out and the aëration continued for forty-five minutes longer. The blood-pressure was then 153 mm. and the carbon dioxide content of the arterial blood was 38.8 volume per cent. The intestines were then handled and in ten minutes the blood-pressure had fallen to 80 mm., and in twenty minutes to 56 mm. After even ten minutes longer there was 31.6 volume per cent. of carbon dioxide in the arterial blood.

As a check to this experiment another experiment was performed. The abdomen was opened by cutting away the anterior wall. The in-

testines were exposed by cutting away the omentum and warm, moistened air passed over them. A long tube was inserted into the trachea in order to preserve the normal amount of carbon dioxide in the blood. At the end of one and one-half hours the blood-pressure had not changed and the animal was in good condition. The intestines were then handled and in ten minutes the blood-pressure fell from 122 mm. Hg to 60 mm. Hg. The carbon dioxide content was 45.1 volume per cent. In twenty-five minutes the blood-pressure was 46 mm. Hg, the carbon dioxide still undiminished and the dog was in pronounced shock. The sciatic nerve was then stimulated and a rise of blood-pressure to 96 mm. Hg was obtained, showing a strong medullary reaction.

These experiments, investigating the relative effects of aërating the intestines and of handling them, justify the conclusion that the manipulation of the intestines and not a diminution of carbon dioxide is the important factor in the causation of shock accompanying exposure and handling of the intestines. We have been unable to find any record among the experiments of Henderson of the production of shock by aërating the abdominal cavity alone within reasonable lengths of time.

#### SHOCK AND MANIPULATIONS OF THE INTESTINES.

In attempting to investigate the mechanism of shock produced by prolonged handling of the intestines, we first sought to establish definite controls. After some preliminary experiments we demonstrated that by handling the intestines violently for one hour, with, it should be remembered, complete anæsthesia, a deep degree of shock could always be produced. In some of these animals the degree of handling of the intestines was sufficient to produce actual rhexis from the peritoneal surface. In our subsequent work we attempted to avoid such a severe degree of handling. We aimed to secure a very intense congestion without actual rhexis. We satisfied ourselves that this degree of handling, in two hours' time could be counted on to produce fatal shock.

Having established this fact we next attempted to discover how far it would be possible to resuscitate dogs from a condition of otherwise fatal shock produced in this manner by transfusion from another dog.



Deep degrees of shock were produced by handling the intestines in six dogs, as described before, for two hours. At the end of this time each animal was in a deep degree of shock. Their eyes were immovable in the orbits and drawn down and inward beneath the conjunctiva. They were absolutely irresponsive to sensory stimulation. Their muscles were relaxed, respiration was shallow, the surface of the body cold, and the pulse rapid and diminished in amplitude. In one of the dogs the transfusion was given immediately after the period during which the intestines were handled, in the others it was given at varying intervals up to one hour after the intestines were handled. Recovery from the shock followed transfusion in all of the dogs. In four of them immediately after the transfusion their eyes regained the normal position in the orbit. The recti muscles of the eyes recovered from their previous relaxation. The dogs voluntarily moved their legs and became responsive to external stimuli. Immediately after the transfusion three of them ran around the laboratory so that they were obliged to be tied up in order to keep them confined. Running around seemed to cause them no discomfort whatever. In two of the dogs which were not transfused until an hour after the experiment, and with which the blood-pressure had been allowed to reach a very low point during this hour, the recovery was less complete, though unmistakable. Following this improvement all of the dogs remained for a long time in about the same condition but permanent recovery was never obtained. They gradually manifested signs of increasing abdominal distress, becoming in consequence more quiet, and died some time during the following night. The temporary improvement after the transfusion described was only the well-recognized improvement regularly following transfusion in shock from any cause. Nevertheless we believe that these transfusion experiments on animals in shock from evisceration of the intestines afford information regarding the nature of shock when carefully studied themselves, and when taken in connection with the control experiments and other experiments about to be described.

The first significant fact to note, and one previously emphasized by Howell and Meltzer, is the comparatively high blood-pressure at the end of the period of intestinal manipulation. Only two of the animals had a blood-pressure approximating 50 mm. Hg. In all the other animals the reduction of the blood-pressure had been as follows: from 104 to 90; from 114 to 54; from 119 to 75; from 115 to 46, and from 105 to 80. The same failure of the blood-pressure during the period of the production of the shock to fall to a dangerously low point was noted in the control experiments; namely, from 116 to 84; from 118 to 67; from 110 to 94; from 102 to 90; from 145 to 88, and from 129 to 101. The one animal



which recovered ran around the laboratory in an apparently normal condition with a blood-pressure of 50 mm. Hg.

These facts demonstrate that at the end of the period during which the intestines were handled the nerve centres must have been supplied with sufficient blood to enable them to functionate properly in the absence of any other disturbing factor.

The second significant point was the very rapid recovery by the animal of his normal condition after transfusion. In other words, an animal in a deep degree of shock which our control proved would have certainly died in a few hours' time with a progressively falling blood-pressure, and in a number of instances with a blood-pressure which had already shown the first steps of this progressive fall, could immediately be resuscitated by transfusion. This rapid recovery precludes the idea that the other disturbing factor to which reference has just been made was an exhaustion of the nerve centres. We cannot conceive of an exhausted centre recovering so quickly. The fact that in our experiments the dogs spontaneously got up and played around and responded normally, as they did, to whistling, indicates that their cortical centres had not been exhausted by sensory impulses. There is no reason to assume that these impulses evoke a greater response in the medullary centres than in the cortical centres. Our deduction, therefore, that the medullary centres were not exhausted or even fatigued is justified. We draw no distinction except in degree between exhaustion and fatigue.

This conclusion is in accord with the results of Porter's experiments which furnish strong evidence that the medullary centres are not exhausted in shock. Porter obtained in numerous experiments a greater percentage rise of blood-pressure by stimulating the sciatic or vagus or splanchnic, or a greater percentage fall by stimulating a depressor nerve after the blood-pressure had been reduced in shock than before the shock had been produced. With a low blood-pressure the same strength of stimulus would probably be more effective both because the vessels may be dilated and because their walls

meet less resistance during contraction. Nevertheless, the absolute rise or fall in Porter's experiments was very great and the experiments furnish strong evidence of the absence of fatigue in the primary stages of shock.

In one experiment we have confirmed the results of Porter's work. A dog was thrown into deep shock by one and one-half hours of violent artificial respiration. On afferent stimulation of the vagus, or sciatic, or stimulation of the splanchnic, a percentage rise of blood-pressure of almost 100 could be obtained. The absolute rise was practically the same as at the beginning of the experiment before the shock had been produced, namely, 30 mm. Hg.

Those who have explained shock as primarily an exhaustion of the nerve centres assume that the blood-pressure in an unconscious animal falls because the medullary centres respond to afferent sensory stimuli and thus dissipate their energy. Numerous experiments have been reported by others in which animals have been thrown into deep shock by prolonged crushing, tearing, and electrical stimulation of sensory nerves. The results of these experiments have been interpreted as demonstrating the power of prolonged and strong afferent stimulation to exhaust the nerve centres. They have been used to explain the shock following serious injuries or operations and of the various methods of producing experimental shock. If, however, these results are used to interpret other forms of shock, they should parallel, particularly as regards time, the actual conditions of the accidents, operations or experiments which they are used to explain.

We have performed experiments of this kind. The animals have received the usual dose of morphin which has been used in all the work presented in this paper. They were then etherized. The sciatic and brachial nerves were dissected out and a strong faradic current applied for two hours to the nerves. Much tearing and crushing of the nerves was incidental to the experiments. During the period of stimulation the medullary centres were certainly active and presumably dissipating energy. This was proved by the hyperpnœa and rise of blood-pressure maintained during the experiment. As soon as the stimulation was discontinued there was a definite fall of blood-pressure, never, however, to a degree which either indicated shock, or could be of any significance in its pro-

duction. The blood-pressure averaged, for instance, at the start of the experiment, during the period of stimulation and after the latter was discontinued respectively 150, 120 and 110 in the first animal; 90, 120 and 100 in the second; 130, 176 and 140 in the third, and 96, 116 and 74 in the fourth.

These dogs required considerable ether, which regularly lowered the pressure each time it was applied. At the end of the experiment all four dogs recovered promptly. Immediately after the experiment the frequency and amplitude of the pulse was good. It compared favorably with that at the beginning. In one hour's time one of the dogs responded normally to his environment; the other three in four hours' time.

There was certainly little difference in this manner of recovery from that which would be presented by another animal which had received an equal amount of morphin and ether.

These statements are emphasized by the differences presented by animals in which the same prolonged severe stimulation of the sciatic and brachial nerves was conducted after the animal had lost the power of controlling his blood-pressure by a preliminary division of the great splanchnic nerves. Three of these experiments were performed. In one animal at the end of fifty minutes' stimulation the blood-pressure had fallen to 14 mm. Hg, death following a short time later. The second withstood a continuous stimulation for two hours; at the end of this time the blood-pressure was 77 and the animal was in deep shock; in three hours' time he was in still deeper shock and he was killed in five hours' time. The third animal recovered from the immediate effects of the experiment.

The relation of diminished blood-pressure to the production of shock in association with the stimulation of sensory nerves was intensified by bleeding the dogs after the splanchnics had been divided. One of these experiments was performed after division of both splanchnics, 200 c.c. of blood were withdrawn, reducing the primary blood-pressure from 152 to 70. The sciatic and brachial nerves were then stimulated as in the preceding experiment. The animal died in deep shock before the conclusion of the experiment.

In four other experiments dogs were bled until the blood-pressure fell to a degree comparing favorably with the fall produced by dividing the splanchnics and the sciatic and brachial nerves were then stimulated for two hours. All four

of the animals developed deep shock; one of them recovered with the aid of an infusion and was alive the next day; another recovered spontaneously, though he did not stir when disturbed; another died during the experiment from excessive anæsthetization, and the fourth succumbed from the experiment. On the other hand, animals subjected to similarly caused reduction of blood-pressure and equal periods of anæsthetization by ether, but not to the prolonged sensory stimulation, suffered from a degree of shock which we were unable to distinguish from that of the stimulated animals which were similarly bled. It must be remembered in this connection that the latter required more ether. We have performed three such control experiments and are satisfied as to the truth of this statement.

As soon, however, as the animal's blood-pressure was reduced and the animal was deprived of his power of compensating for lowered blood-pressure by paralysis of the splanchnic area, serious shock developed but always in proportion to the diminution of blood-pressure and not greater than in animals in which the blood-pressure was reduced to a similar degree by hemorrhage alone.

In shock produced by prolonged handling of the intestines it seems that much less severe sensory impulses can be present than occur in stimulation of the sciatic and brachial plexus for the same length of time. Consequently, if sensory impulses in an unconscious animal were not effective in producing shock by causing exhaustion of the central nerve cells in the absence of vasomotor control, it is not likely that they are the important factors in the production of shock by prolonged handling of the intestines. Simple division of the splanchnic, as we ourselves have also experienced, does not in itself result in a lowering of the blood-pressure sufficient to produce shock. Within the time limit which we have adopted in these experiments, which is quite sufficient from the practical point of view of the operating surgeon, the exhaustion of the nerve centres by afferent stimulation of sensory nerves is a wholly negligible factor in the production of shock.



CAUSE OF SHOCK PRODUCED BY MANIPULATION OF THE  
INTESTINES.

Returning again to the interpretation of the experiments in which shock was produced by prolonged handling of the intestines and in which attempts were made to resuscitate the dogs by transfusion, the quick recovery precludes the idea that the nerve centres had been exhausted. It does not, however, negate the possibility of the condition of the animals at the end of the period of intestinal handling being due to cerebral anæmia in combination with the anæsthesia which had been used. While the blood-pressure was still far above a level which would prostrate an animal wholly out of anæsthesia, there was little difference in the condition of these dogs and similarly anæsthetized dogs whose blood-pressures had been reduced to a similar degree by hemorrhage. Cerebral anæmia, however, is a far different condition from exhaustion of the nerve centres, a state demonstrated to be absent, as we have repeatedly emphasized, by the rapid recovery after transfusion.

But as has been stated, with the fairly high blood-pressures recorded in these experiments cerebral anæmia could have contributed little to the degree of shock exhibited by the animals. Many facts indicate that coöperating with the cerebral anæmia, inhibitory impulses are important causes of the animal's condition at the end of the period during which the intestines are handled. On the cessation of the handling there would be a return of a reflex response of the animal indicating semiconsciousness. An immediate relapse into an insensitive comatose condition could be produced by continuing the handling. The blood-pressure usually fell when the handling was stopped and rose again under the stimulus of handling, though this was not a constant effect. We know that afferent impulses of possibly an inhibitory nature are present. It is due to them that these experiments of evisceration and intestinal manipulation may be performed at times without the continuous use of a specific anæsthetic other than morphin and the preliminary anæsthesia, and yet without any evidence whatever of feeling on the part of the animal. There



is no physiological reason for distinguishing between shock and collapse. The latter condition is entirely due to inhibition. Howell and Meltzer have presented additional evidence that inhibitory impulses are important factors in this stage. They unquestionably are responsible in the beginning of the experiment for the onset of shock and the first fall of blood-pressure. If they are then operative they must continue to be during the whole time during which the intestines are handled.

Following the period during which the intestines were handled in those animals in which the shock was produced for control purposes and which were not therefore transfused, there occurred a progressive fall of blood-pressure within the next few hours until death occurred. The progressive fall was often initiated by a considerable drop at the start. This progressive fall was unquestionably due to bleeding into an absolutely paralyzed splanchnic system. During this period we have found that stimulation of the splanchnic nerves produced no rise in blood-pressure, or change in a plethysmographic tracing measuring the amount of blood in the splanchnic area. There were even no indications of blood-flow through the intestinal vessels.

The local peripheral character of this vascular paralysis has been clearly shown by two experiments. A coil of intestines was protected in a plethysmograph during a period of handling of the intestines for one hour and one and one-half hours. The splanchnic nerve was stimulated and the diminution of volume within the plethysmograph recorded before and after the period during which the intestines were handled.

The protected loop and kidney showed a marked change in volume both before and after the period of intestinal manipulation, while after this period a loop of the handled intestine showed no change.

There can be no question therefore about the extreme paralysis of the splanchnic area after two hours' handling of the intestines. There is an absolute paralysis of every tissue of the intestines, of the muscles, of the intestinal walls and of the arterioles. There is an absolute abolition of all reflexes. The great means by which vasomotor changes in the body are

possible, that which the vasomotor centre uses to produce its rise and fall of pressure and without which it is powerless, is hopelessly unavailable.

The amount of blood which this area will contain is well illustrated by a number of experiments which we performed, in which during the period of handling the intestines, the brain of the same animal was supplied with blood from the carotids of another dog, and in one case from the carotids of two other dogs. Before the intestines were handled, an anastomosis was made between the carotids and external jugular veins of the donor and the recipient, which was to be shocked. The purpose of these experiments was to discover whether or not any diminution of shock could be obtained by supplying the dogs being shocked, with blood from a presumably normally beating heart, thus eliminating the small fall in pressure occurring in the other transfused dog, during the experiment. In general the dogs gave the same result as the dogs transfused at the end of the experiment. The main purpose of the experiment was defeated, however, by the fact that the splanchnic area of the recipient during the period in which the intestines were handled drained off so much blood from the donor and in one case from two donors, that the blood-pressure of all donors in the three experiments fell to a serious degree, so that at the end of the experiments the donors no longer supplied the brain of the recipient with blood under good pressure, and were themselves in a serious condition from exsanguination.

Animals shocked in the manner described are deprived of all vasomotor control solely because of a local peripheral paralysis of the splanchnic area. It is as though the branches of their mesenteric arteries emptied into a large reservoir with perfectly flaccid walls, into which they bled to death. The aptness of the comparison of the splanchnic area to a flaccid rubber bag is made more apparent by pressure on the abdomen. The blood-pressure can be raised at will by this procedure. The explanation of the secondary shock developing in the transfused animals, the intestines of which are paralyzed from one end to the other, introduces very complex questions which

are not concerned in this paper. Suffice it to say that the animals remained in good condition with high blood-pressure in one case—the only dog watched till death—for twelve hours, and that they rather suddenly passed into a moribund condition.

#### CONCLUSIONS.

Our conclusions, which we hope to support by more numerous experiments, and by reporting them in greater detail in the future than has been possible in this paper, are as follows:

1. As severe a degree of shock may be produced by artificial hyperrespiration, and by handling of the intestines when provision is made for keeping the carbon dioxide content of the blood high, as when it is allowed to fall to 40 or 50 per cent. of the normal.

2. Shock produced by artificial hyperrespiration is due chiefly to a long-continued, mechanical interference with the return of the blood to the heart.

3. There is evidence that the early stages of shock produced by evisceration and handling of the intestines is due to inhibitory afferent impulses.

4. At the end of the period during which the intestines were handled none of the animals' nerve centres were exhausted.

5. By such handling of the intestines a complete splanchnic paralysis of local peripheral origin is produced, and it is this paralysis which causes the subsequent fatal fall of blood-pressure and not exhaustion of the nerve centres.

6. In the presence of a good blood-pressure and unimpaired vasomotor compensatory mechanism, prolonged afferent electrical stimulation for two hours will not produce shock or exhaustion of the nerve centres.

7. If trauma to the sensory nerves is a factor in production of shock in an unconscious animal, it is wholly subsidiary to other factors, and it is questionable whether it was apparent in our experiments even when these other factors had rendered the nerve centres more vulnerable by toxic influences, as ether, or by a fall in blood-pressure.

8. The all-important factor in the development of shock, in so far as the forms which we have studied may represent shock in general, is loss of vasomotor control. It is, at least, the impossibility of regaining this control after it has reached a certain degree which determines the failure to recover. The mechanism of this loss and its maintenance is important. The loss of control and its maintenance is never caused by acapnia or central nervous exhaustion, but, aside from afferent impulses more especially splanchnic sensory impulses which may have initiated the shock and contributed to it, the loss of control was always due to local peripheral causes which in our work were mechanical obstruction, loss of blood and trauma to the viscera.

The practical conclusions from these observations emphasize the necessity, in attempting to prevent shock, of providing against a fall of blood-pressure and local trauma, particularly within the abdomen, as the most important of all precautions. The truth of this statement at present is so generally acknowledged that it is almost trite to make it. Nevertheless the conclusions, indicated by the experiments in which unsuccessful attempts were made to produce shock by trauma to peripheral sensory nerves, will not be generally accepted. They directly contradict grounds on which the method of anæsthesia known as anoci-association is based. We appreciate that our experiments are few. Nevertheless, a study of their details demonstrates that their results were decisive and that severe trauma both electrical and mechanical of peripheral somatic nerves in an unconscious animal within reasonable time limits did not result in either a reflex fall in blood-pressure or exhaustion of the nerve centres. Its influence as a cause of shock at least in so far as the three forms of shock which we have studied may serve as examples of shock in general is so small that it may be practically neglected. In this connection it must be remembered that shock following burns is toxic in its nature.

However valuable the blocking of sensory nerves during operation may prove, the explanation is not to be found in the protection which it may insure against fatigue of the nerve



centres, certainly within the time limits of the usual operation. It is doubtless a wise precaution, on account of the more complicated manner in which reflexes may be modified in the human being than in animals, to block the larger trunks of the sensory somatic nerves when these must be divided. Clinical experience certainly teaches that it is most desirable to block the sensory splanchnic nerves when their trunks or more particularly the region of their plexuses must be subjected to trauma. Such blocking will often spare a patient reflexes which may seriously lower the blood-pressure. But the harmful effects, if it persists, is not due to fatigue of the nerve centres but entirely to reflexes and peripheral changes which may be either secondary to them or the result of other local peripheral causes or both. It is equally important to recognize that vasomotor control may be impaired or lost by peripheral injury alone. The central mechanism seems capable of outlasting the peripheral mechanism every time.

The necessity of guarding against loss of blood is self-evident. Of equal importance is the selection of an anæsthetic which, aside from any consideration of toxicity, does not reduce blood-pressure. Ether does not always fulfil this condition. Clinically and experimentally, unless administered with the greatest care, it strongly reduces the blood-pressure. We have numerous illustrations of this fact among our tracings and are disposed to attribute much of the shock of long operations under ether to this fact and to its toxic effect on nerve tissue and the glandular organs. Nitrous oxide does not possess this disadvantage and is also much less toxic. Crile has in no instance shown his keen appreciation of those factors which make surgery more successful than in his advocacy of nitrous oxide anæsthesia. If the general blocking of sensory nerves only increases the efficiency of nitrous oxide anæsthesia it is for this reason valuable. Its effect in eliminating harmful reflexes caused by trauma, particularly in the region of distribution of the splanchnic sensory nerves, has been explained.

We desire to thank Dr. Holmes C. Jackson and Dr. Fred-eric S. Lee for helpful suggestions and criticisms.







## THE RELATION OF ACAPNIA TO SHOCK, AND A CONSIDERATION OF THE MECHANICAL EFFECTS OF ARTIFICIAL HYPER- RESPIRATION UPON THE CIRCULATION

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It has been claimed that the most important factor in the causation of shock is diminution of the carbon-dioxide content in the blood and that this diminution is a regular consequence of all influences resulting in shock. That carbon dioxide exercises significant physiological functions cannot be denied; determination, therefore, of the true significance of the diminution of its normal proportion in the blood is important and bears a special relation to the various methods of artificial respiration utilized in thoracic surgery.

This study was undertaken for the purpose of investigating the relation of acapnia to shock. All experiments were performed on dogs.

The *first series* of experiments was conducted for the purpose of studying the effect of variation in intrapulmonic air-pressure upon the blood-pressure. The thorax was opened laterally, a T-tube connected with a water-manometer was tied in a small bronchus, and the heart enclosed in a Henderson cardimeter connected with a recording tambour. The blood-pressure was recorded from the carotid artery. The thorax was then closed and intratracheal insufflation was given from an apparatus provided with an exhaust valve, which reduced the pressure to approximately zero from four to twelve times per minute. When the machine was running at a pressure of 6 mm. of Hg there was an average rise of blood pressure of 15 mm., each time the exhaust valve operated.

<sup>1</sup> The work presented in this paper was begun in the Laboratory of Biological Chemistry of Columbia University, at the College of Physicians and Surgeons; BIOCHEMICAL BULLETIN, 1912, ii, p. 175.

In one experiment with an increase in intrabronchial pressure of from 8 to 30 mm. Hg, the blood pressure fell from 122 to 55 mm. Hg, and the volumetric tracing indicated that the output from the heart had diminished about 44 per cent. These variations in blood-pressure were completed within a few seconds after the change in intrabronchial pressure, and could be duplicated at will. A rise of intrabronchial pressure above 8 to 10 mm. Hg always caused a fall in blood-pressure and it was concluded that the variation in pressure was the result of a diminution of the venous return to the heart, resulting from compression of the veins in the thorax. In view of the marked changes in the blood-pressure and output of the heart resulting from small variations in intrapulmonic pressure, it is evident that, in any experiments planned for the purpose of estimating the part played in the production of shock by a diminution of carbon-dioxide content, induced by artificial hyper-respiration, the effects of the increase of intrapulmonic pressure upon the return flow of blood to the heart must be considered.

With the *second series* of animals, Henderson's experiments were duplicated, the dogs being artificially respired by means of a force-and-suction pump, working about seventy times per minute. The animals were given morphin, and ether was administered only when necessary. In these experiments, blood-pressure fell about 40 per cent. within one minute after artificial respiration was begun, and then decreased more slowly throughout the experiment to between 40 and 50 mm. Hg. At the end of the experiment, when the artificial respiration was stopped, the blood pressure increased 60 to 90 per cent. within a few seconds. In all experiments the blood analysis showed that the carbon-dioxide content, at the end, was only 40 to 50 per cent. of the original amount. These animals, at the end of two to three hours of artificial respiration, were all in a condition of deep shock. This degree of shock was indicated by a rapid pulse, a low blood-pressure, and a marked degree of insensibility to sensory stimulation. Three of the animals so treated lived three days (dying of secondary effects of the experiment), and one lived twenty-four hours. None of them died from the immediate effects of the experiment. During these experiments, when the artificial respiration was interrupted or permanently

stopped at the end of the experiment, the period of apnea lasted only one or two minutes, so that no death resulted directly from asphyxia dependent in turn upon acapnia. The absence of a prolonged period of apnea is explained by the fact that the effect of ether was not added to that of morphin.

With a *third series* of animals the experiments just described were duplicated, with the exception that the carbon-dioxide content of the blood was maintained at its normal level, or slightly above it. The conservation of the carbon dioxide was accomplished by inserting a large rubber bag, to act as a reservoir, between the suction pump and the force pump, thus creating an almost perfectly closed circuit; the dog thus rebreathed expired air. To replace the small amount of air and carbon dioxide lost from the animal's trachea, carbon dioxide was administered from a tank into the rubber bag, where it mixed with air drawn in from the trachea. In these experiments the animals went into the same degree of shock in two or three hours as those of the second series, in which the carbon-dioxide content of the blood was diminished to 40 per cent. of the original volume. One animal died on the table just before the completion of the experiment, the others lived for from one to three days. Blood-pressure changes in the two series were similar but a characteristic of the experiments, in which the carbon-dioxide content was kept at or a little above the normal, was a less rapid and weaker heart-beat than that observed when the carbon-dioxide content was diminished.

No other conclusions can be drawn from the experiments of Series 1 and 2 than that the reduction in the carbon-dioxide content of the blood was not an important factor in the causation of shock produced by hyper-respiration, and that in shock so produced, the essential factor was an interference with the venous return to the heart.

In the *fourth series* of experiments the effects of aerating and handling the intestines were studied. A celluloid window was placed in the abdominal wall, and a stream of warm moistened air was passed over the intestines for a period of three hours. During this procedure the animals breathed normally, the blood-pressure was 163 mm. Hg, the content of carbon dioxide was slightly



diminished, and there was no evidence of shock. Beneath the celluloid the absence of peristalsis could be observed as well as the efficiency of the aeration and failure of the intestines to become dry. The celluloid was then removed, the intestines spread out, and the aeration continued. After 45 minutes the carbon-dioxide determination indicated a content of 38.8 vol. per cent., and blood-pressure was 153 mm. Hg. The intestines were then handled; in ten minutes blood-pressure had fallen to 98 mm., in twenty minutes to 56 mm. Hg, and in forty minutes there was still 31.6 vol. per cent. of carbon dioxide in the arterial blood.

In another experiment the intestines were exposed and aerated (not handled). The carbon-dioxide content of the blood was maintained by connecting a long tube with the trachea. After one hour and a half, blood-pressure had changed but 1 mm. Hg, and the animal was in good condition. The intestines were then handled and in ten minutes the blood-pressure fell from 122 to 60 mm. Hg. The carbon-dioxide content was 45.1 vol. per cent. In twenty-five minutes the blood-pressure was 46 mm. Hg, the carbon-dioxide content normal, and the dog in a severe degree of shock.

In these abdominal experiments the primary factor concerned is unquestionably the manipulation of the intestines and not any diminution of carbon-dioxide content caused thereby. It will be remembered that in the similar experiments with aeration of the intestines reported by Henderson, the intestines were handled gently. We have been unable to find any mention in his paper of aeration of the abdominal cavity with air alone beneath a celluloid membrane as a control.

Henderson's control experiment, in which he did not secure shock, included aeration (with a stream of air plus carbon dioxide) of the abdominal cavity beneath a celluloid window in the abdominal wall. Our own experiments show that aeration of the intestines without the addition of carbon dioxide does not produce shock.

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**THE CONSERVATIVE TREATMENT OF INTRINSIC CANCER  
OF THE LARYNX BY THYREOCRICOTOMY (TOTAL  
LARYNGOFISSURE) OR THYROTOMY (PARTIAL  
LARYNGOFISSURE)**

**BY GEORGE DAVID STEWART, M.D.**

**OF NEW YORK**

**SURGEON TO BELLEVUE AND TO SAINT VINCENT'S HOSPITALS**

THE treatment of malignant growths in regions where the lymphatics are abundant and lymphatic drainage territories ill defined, has shown in recent surgery two distinct tendencies: one to a radicalism that is disabling, the other to a conservatism that is merely palliative. The *former* tendency is well illustrated by the so-called block dissections, in which, for cancer invading the tongue, it is recommended to remove that portion of the inferior maxilla and floor of the mouth contiguous to the site of the lingual lesion, and, in addition, all the glands in one, sometimes both sides of the neck. This is a serious operation, the disfigurement after healing is severe and distressing, and often both surgeon and physician are disappointed to find the growth has recurred in the scar or in some lymphatic node that has escaped observation or is inaccessible. The *latter, i.e.*, the conservative course, is adopted by many surgeons who feel that, in tongue cancer, for instance, if the disease cannot be removed with a fair degree of thoroughness by an operation of moderate extent, it is better to attempt none or only palliative surgical measures.

The treatment of cancer of the larynx will follow one or the other of these courses, depending on whether the disease is extrinsic or intrinsic. In *extrinsic* cancer (Fig. 1), *i.e.*, growths located on the interarytenoid space, aryteno-epiglottic folds, epiglottis, or pyriform fossæ, the disease spreads rapidly, metastases occur earlier, and for their radical removal a complete laryngectomy after the method of Glück or some modification of that method is demanded. This operation is severe, crippling, destroys the voice, and is comparable to the block dissections referred to. While recurrences frequently follow, still the results in complete laryngectomy appear to be much better than those following operation of the tongue, for example; due in part, at least, to the fact that cancers of the larynx soon give evidence of their presence by definite symptoms relating to the voice or swallowing. Further, they are watched by skilled specialists and detected in their incipient

stages, while mouth, tongue and cheek cancers often remain under the care of the family practitioner or are for some time disregarded entirely. Most important, however, is the lymphatic distribution, to be referred to later, which is so arranged that for a long time complete removal is possible.

*Intrinsic* cancer, on the other hand (Fig. 1), *i.e.*, cancer located on the true or false cords or somewhere below that level, is amenable to comparatively simple surgical procedures without great crippling and with a certainty of cure that surpasses cancer in almost any other situation—facts first demonstrated by Butlin and Semon, and more recently by an increasing number of observers with almost constantly improving statistics.

It is the purpose of this short paper to restate and emphasize the value of conservative surgery in the treatment of these *intrinsic* cancers, to point out that the work may be undertaken by the general surgeon in conjunction with the laryngologist, to briefly describe the steps of the operation and to report several cases illustrating the good results that may be expected.

The *lymphatic* vessels (Figs. 2 and 3) and nodes of the larynx, which, no doubt, play a most important part in the dissemination of cancer, are described by Most as follows: The network of lymphatic vessels in the larynx is separated almost entirely into a supra- and subglottic area by a horizontal non-vascular streak, a sort of *lymph-shed*, following the vocal folds (cords) (see Fig. 2). The only lymph-vessels connecting the two areas are those forming a rather rich network in the mucosa of the posterior laryngeal wall.

The supraglottic lymphatic area is somewhat richer than the subglottic, being more fully developed in the ventricle of the larynx and upon the ventricular folds (false vocal cords) than elsewhere. Above it is continuous with the lymphatic network of the epiglottis; below it is continued into the subglottic area by means of the vessels in the mucosa of the posterior laryngeal wall. The network becomes very scanty upon the upper surface of the vocal folds and upon their free margins is lost altogether.

The subglottic lymphatic area consists of more delicate vessels than the supraglottic, although, in general, the meshes are somewhat closer. Below it is continuous with the tracheal lymphatics; above it is continued posteriorly into the supraglottic area, but latterly it is lost at the summit of each vocal fold.

From the supraglottic lymphatic area, three to six efferents pass from the lateral region of the epiglottis at the aryepiglottic folds. These

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pass through the hyothyroid membrane, and, reduced in number by coalescence, follow the superior laryngeal artery and cross the external carotid. They join the group of deep cervical glands situated on the common facial and internal jugular veins, or upon the thyroid gland. Some of the vessels occasionally pass *via* glands placed upon the intermediate tendon of the digastric, or at the lateral margin of the thyrohyoid muscle.

From the subglottic area, the vessels emerge in two sets: from the anterior subglottic area a few fine vessels pass through the conus elasticus (cricothyroid membrane) either in the midline, or laterally accompanying the inferior thyroid artery. The lymph from these eventually enters the deep cervical glands. The first vessels go to a pre-tracheal gland lying upon the conus, from which efferents may pass to a lower pre-tracheal gland and from the lower (when present), to a gland situated about the middle of the internal jugular vein, and to another pre-tracheal gland below the isthmus of the thyroid.

From the posterior subglottic area three to six vessels pass below the cricoid cartilage through the cricotracheal ligament. The vessels from this area accompany the recurrent laryngeal nerve and reach a chain of peritracheal glands which extend from the cricotracheal ligament along the posterior margin of the thyroid gland. In one case, Most found a vessel passing to the pre-tracheal gland upon the thyroid isthmus.

Thus intrinsic cancer remains for a long time confined to the inner surface of the organ, because of the scanty lymphatics and the restraining influence of the cartilages. The vessels do not enter these cartilages but are directed by them through the intercartilaginous membranes; thus there is slow absorption. When lymphatic drainage does take up the new growth, it follows certain lines, invades definite nodes, and, although it becomes extrinsic, there is still great good to be expected from the more radical operations.

Apart from the influence of the lymphatics, it is held by some that intrinsic cancer of the larynx is essentially a slow growing neoplasm.

It is important, in order to obtain the best results, that an early and definite diagnosis be made, and this can be done only by one thoroughly skilled in the use of the laryngeal mirror, and in the removal, by intralaryngeal methods, of portions of the growth for microscopic examination. When the growth is on the centre of the cord, as it is in more than one-half the intrinsic cases, the diagnosis is easy enough, but when it is under the cord, it can with difficulty be seen, its extent cannot be ascertained, and it is also difficult to remove a satis-



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factory piece for examination. It is then probably better to do a thyrotomy, remove the growth, and afterward make certain of a diagnosis, than to wait until the case has become extralaryngeal. In my cases, diagnoses were all made by Drs. Coakley and Chisholm, the former taking specimens for examination in each case.

### TECHNIC OF THE OPERATION

Many operators advise local anæsthesia. In one of the cases reported herewith, it was utilized for the preliminary tracheotomy, further operation being continued under chloroform administered through the tracheal cannula; in the other two, chloroform was administered from the outset. One of the advantages of local anæsthesia is that during the operation the sensibility of the larynx is in some degree obtunded, reflex acts of coughing are lessened, and, following the operation, the conduction of pain to the central nervous system is controlled, a point worthy of consideration, since the shock of handling laryngeal tissues, particularly those above the vocal cord, is great. However, to have the sensibilities too much blunted is never an advantage, because of the danger of an aspiration pneumonia, one of the most frequent and serious complications following laryngeal operations. Even when general anæsthesia has been used, it is easy to spray or swab the larynx or pharynx with a four per cent. cocaine-adrenalin solution to prevent the reflex acts of coughing and vomiting which so disturb the conduct of the operation. This can easily be done in general anæsthesia after the thyroid has been opened, is not likely to be carried too far, and should permit the return of sensibility as soon as bleeding has been controlled, or as soon as the thyroid cartilage has been closed, until which time the patient should be kept with the head low to prevent aspiration into the lung.

Some operators prefer general anæsthesia, using chloroform, particularly in elderly people where it is feared to raise the blood-pressure, and on account of the lesser bleeding. In neurotic people there is no more objection to general anæsthesia than in any other condition. Besides, the presence of the tracheal tube allows one to tampon above the tube and thus prevent the entrance of blood into the lungs in a more effective way than can be done under local anæsthesia.

*Tracheotomy* should be performed as a preliminary, either several days preceding—thus making it a two-session operation—or immediately prior to the operation on the larynx. If the tracheotomy is performed some days in advance of the laryngeal operation, the mucous membrane has had time to adjust itself to the altered conditions under



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which it receives the air, there is less coughing, and, in addition, the patient is able to swallow better and earlier following the operation. On the other hand, if the patient is phlegmatic, indisposed to brook the delay, or in fairly good condition, the tracheotomy can be performed at the time of the operation as well as it is in the Glück method of complete removal. It is doubtful indeed if the infliction of the two operations at once is much if any greater than that of a tracheotomy alone.

The location of the tracheotomy should be low, but it will depend on the length of the neck, the depth of the soft tissues, and the location of the isthmus of the thyroid. One skin incision, as a rule, is sufficient for both operations, but it is conceivable that in a very long slender neck there might be two, one for a low tracheotomy and one for the operation proper. In all my cases the incision for the operation served also for the tracheotomy.

One should be prepared with tracheal tubes of different sizes and lengths. One of these should be long and flexible, and the Hahn or sponge-covered tube and the Trendelenburg tampon cannula should both be at hand, although neither may be necessary.

Some do not perform tracheotomy but keep a cannula through the cricothyroid ligament for some days after operation.

The next step is to split the thyroid cartilage in the angle between its two laminae, *i.e.*, in or near the median line, so as to protect the anterior insertions of the vocal folds, and this is by no means as easy as it would appear. This cartilage with the cricoid begins to ossify soon after the twentieth year, and in elderly people, the age at which cancers occur, it is often completely turned into bone, requiring a very strong sharp instrument to sever it. Scissors are recommended by most surgeons, but, as a rule, will be found totally inadequate, and very strong bone cutting shears or forceps will be necessary. The difficulty in the way of using any strong instrument is in introducing a blade, which must be large in order to be effective, through the cricothyroid membrane, without pushing off the lining mucosa and thus detaching the anterior end of the sound vocal cords even if the cord is spared at the time of operation, its attachment may be endangered through subsequent necrosis. In one case reported herewith, this accident happened—the anterior end of the opposite cord was stripped to some extent, was replaced by a stitch, and for a long time afterward showed in the laryngeal mirror as a beginning invasion. The laryngologist who had the case under observation suspected it of being a recurrence until this circumstance was recalled, and this, coupled with the fact that there

was no increase in size, led to the correct conclusion that it was not an extension of the growth.

As one splits upward there is danger of wounding the epiglottis, and, remembering the earlier teaching that the epiglottis closes down over the upper aperture of the larynx during deglutition, it was disturbing to find, in one case, a large rent in the central tendon of this structure. Later teachings, however, are to the effect that the epiglottis is not of great importance in the act of deglutition and can be removed without interfering, in any great degree at least, with the passage of food.

The thyroid having been opened (partial laryngofissure), it is now necessary to tampon the larynx above the cannula and also the pharynx to prevent soiling from the mouth or the œsophagus. Prior to this, it is necessary, if general anæsthesia has been used, to swab the larynx carefully with cocaine-adrenalin solution, as already indicated. If a pack is carried into the œsophagus, it not only prevents soiling but helps to locate the septum between larynx and pharynx.

Sometimes the room acquired by opening and spreading the thyroid is insufficient. It will depend on the angle at which the two laminæ of the thyroid meet. In the adult male this angle is about ninety degrees; in the female, about one hundred and twenty degrees, which means that in the latter it will be more difficult to expose the side walls. If insufficient, it may be necessary to cut the cricoid anterior arch (thyreocricotomy or total laryngofissure) and, although it is best not to do this, no great harm follows the manœuvre.

After the interior of the larynx has been thus exposed so that the growth can be seen in all directions, it should be completely outlined by a knife, cutting down to the cartilage about one centimetre beyond the edge of the growth, then the diseased tissues should be taken away with a sharp periosteal elevator and short strong scissors markedly curved on the flat.

To determine how deeply one should go I have had some frozen transverse sections made (Figs. 4, 5, 6, 7, 8 and 9). By reference to these, it will be seen that at the front and sides the tissues can be peeled cleanly from the inner surface of the thyroid cartilage, in the lower posterior part from the inner surface of the cricoid ring, that is, the dissection should be subchondral. Higher, at the level of the arytenoids, it is necessary to exercise care. If the growth is limited to the centre of the cord, it will only be necessary to cut the posterior end away from the vocal process of the arytenoid. If it extends further back, involving the vocal process, a part or whole of the arytenoid on that side should be

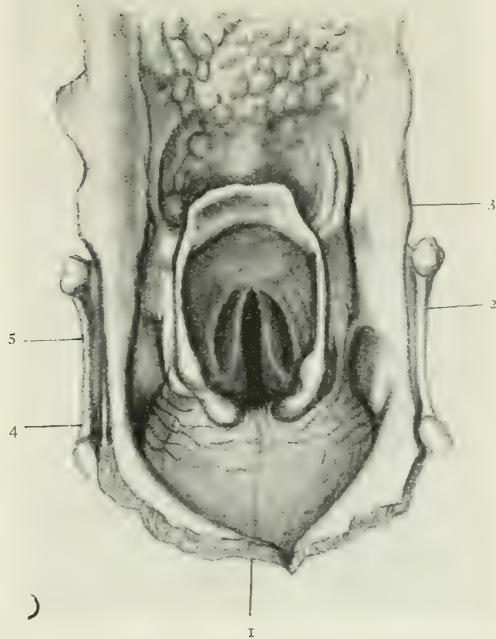


FIG. 1.—Extrinsic cancer is located at 1, interarytenoid space; 2, aryteno-epiglottic folds; 3, epiglottis; 4, pyriform fossæ. Intrinsic cancer is located at 5, vocal fold is somewhere below that level. (After Cunningham.)

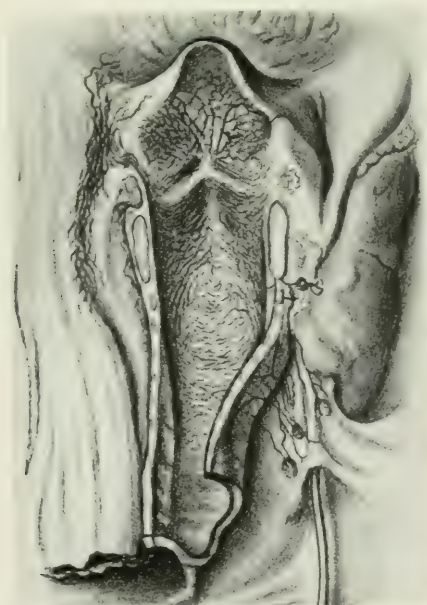


FIG. 2.—Showing network of lymphatics in interior of larynx (see text). (After Most.)

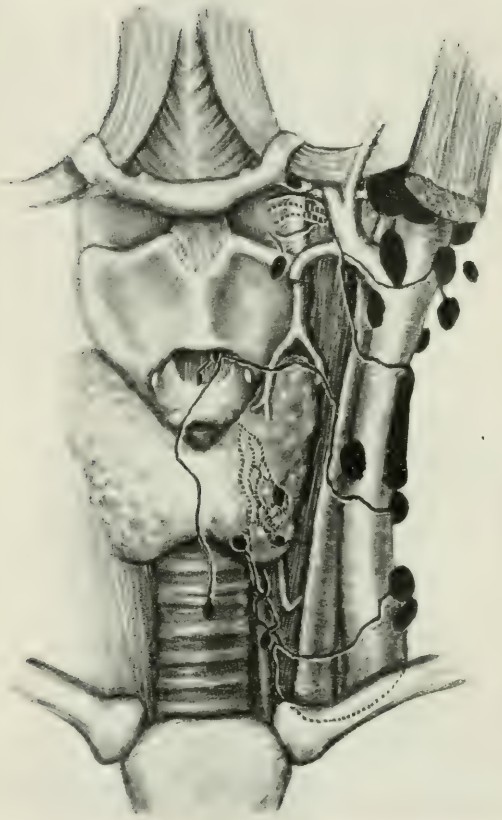
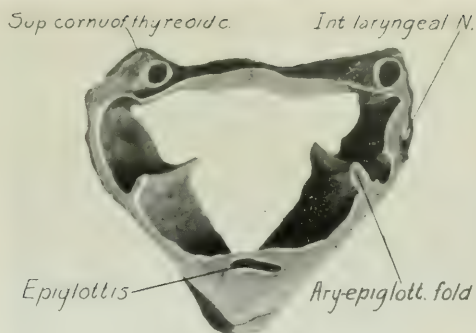
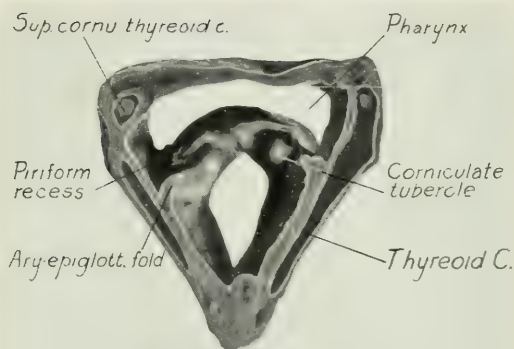


FIG. 3.--Showing exit of lymph-vessels from larynx and the nodes into which they empty.  
(Adapted from Keen's Surgery, after Most.)



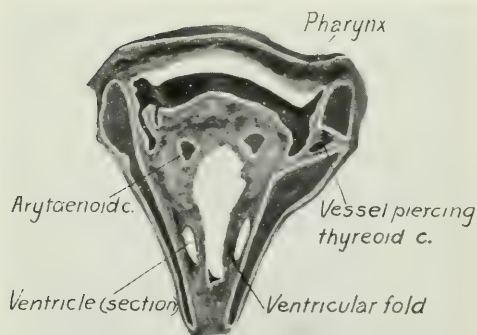
— 1. DISC 5-6C. —

FIG. 5.



— 2. 6C. VERT. —

FIG. 6.

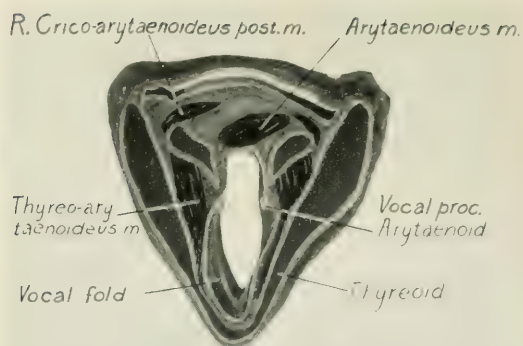


— 3. DISC 6-7C. —

FIGS. 4-9.—(Original.) Transverse sections of larynx at different levels. They indicate the depths to which dissections can be carried in dissecting away the vocal cord. Figs. 6, 7 and 8 are particularly useful, indicating where the periosteal elevator and where curved scissors will best serve the operator. For further description see text.

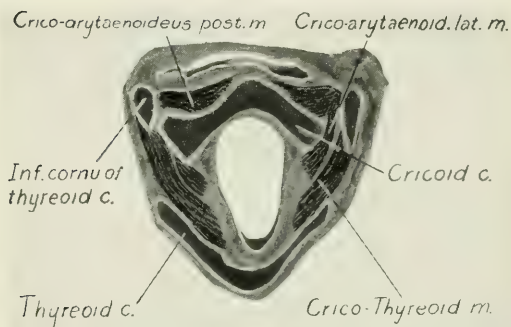


FIG. 7.



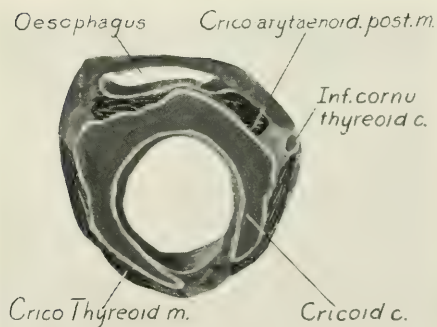
— 4. 7 C. VERT. —

FIG. 8



— 5. DISC 7C-1TH. —

FIG. 9.



— 6. 1TH. VERT. —

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taken away. When the arytenoid is involved, or when the growth crosses the posterior commissure involving the interarytenoid space, the case is not suitable for removal by thyrotomy, but a partial or complete laryngectomy should be performed, a condition for which one should always be prepared beforehand. The lateral muscles which rest under the thyroid on the conus elasticus, particularly the thyro-arytenoid and the conus elasticus itself, will be sacrificed in this dissection.

Control of the hemorrhage, as a rule, is not difficult, and bleeding is usually very much restricted through the use of cocaine and adrenalin. Vessels should be tied or crushed, and sometimes, when a vessel perforates the cartilage, it is difficult to do either, and then it may be necessary to use the cautery, which can be utilized only when local anæsthesia or chloroform has been employed. If absolutely necessary, one may control the bleeding by tamponing the cavity of the larynx, but most authors advise against this, regarding prompt closing as an important part of the operation.

Closing is effected by two or three stitches in the perichondrium and soft tissues, or, if the cartilage is not ossified, the sutures may be made to pass through the cut edges. In ossified cartilage, there is no need to take this precaution. Drainage need not be employed, as a rule, for the wound is very superficial. An attempt to close the defect in the mucous membrane as far as possible is recommended by some.

The after-treatment is to keep the patient with head low until after consciousness has returned, then in the semi-upright posture in a room in which there is plenty of moisture in the air. The tube can be removed in twenty-four or forty-eight hours, if no œdema obstructing the pharynx is present, which may be determined by laryngeal examination, or by taking the tube out and testing it, standing ready to replace it at a moment's notice. The patient should be gotten up promptly, as a rule on the second or third day. Feeding is a difficult problem, because the wounded larynx does not draw up well under the backward protruding tongue during efforts of deglutition. One of my cases, the younger, who was more agile, was able, by putting his head lower than the rest of his body, to drink milk much as it is taken by a dog or cat, when, to do so in the ordinary posture, caused distressing strangulation. It is possible that a preliminary tracheotomy might permit the patient to take food earlier for the same reason that respiration is more easily carried on. When normal acts of swallowing cannot be performed, it may be necessary to feed through the nasal tube.

Necrosis of the edge of the cut cartilage often follows the laceration of tissues, as they are very poorly nourished. One of my cases kept

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on for several months discharging through a small sinus, doing the patient more mental than physical harm. On any account, however, the sooner such a process is over, the better.

The functional results are excellent: The cases I have done talk very well. As to recurrence, in two of them the prognosis is certainly favorable, one having already gone over three years, another nearly that length of time. In addition, I have two other cases, five in all, operated on long ago from which I heard some years later but have recently had no communication.

*Conclusion.*—Laryngofissure is applicable to over one-third of all cases of laryngeal cancer. It is exclusively adapted to endolaryngeal cancer in its incipient stages. A circumscribed movable tumor near the centre of one vocal cord represents the most favorable case for laryngofissure. The operation is sometimes extended to cancer still movable but which has attacked the anterior commissure, the ventricle or the subglottic space. Laryngofissure is absolutely contra-indicated in all cases in which the arytenoid cartilage and the interarytenoid fold are involved, also in other extrinsic cancer. It is not often enough performed and is sometimes attempted too late. Its extent should be absolutely determined beforehand, otherwise one should be prepared for a semi or complete laryngectomy. The mortality is small—0.2 per cent. Speech is always possible, often satisfactory.

CASE I.—W. R. M., insurance broker, aged sixty-four years. Patient always has had a sensitive throat and has had almost constant treatment. Because of increasing hoarseness, he consulted Dr. Stewart, who referred him to Dr. Chisholm in October, 1911. In December, 1911, two specimens were removed by Dr. Coakley for examination. Second specimen was suggestive of malignancy.

*Operation* (January 27, 1912).—The patient had a short neck. The incision was made from the hyoid bone to episternal notch. The isthmus of the thyroid was in the way and was severed between ligatures. A tracheotomy tube was inserted. The thyroid cartilage was split in the median line and the cricoid also to increase exposure. The left vocal cord was trimmed out entirely and its base cauterized. The anterior end of the right cord was also taken away. The mucous membrane in the vicinity of the anterior commissure was also removed.

*Pathological Report.*—Specimen consists of a greatly thickened vocal cord and a small portion of tissue removed from the wall of the larynx.

The vocal cord presents near its centre an irregularly outlined indurated elevation, the surface of which presents several small crypts.

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Microscopical examination of sections made directly through this area reveals the histology of an epithelioma.

Microscopical examination of the small particle of tissue removed from the wall of the larynx fails to reveal evidence of secondary deposits.

Present condition: patient talks fairly and feels better than for a long time. He states that a feeling of stiffness in the throat which has existed for a long time prior to operation has disappeared.

CASE II.—I. J., physician, aged fifty-two years.

*Family History.*—Striking history of malignancy on paternal side; father, one uncle, two aunts, and a cousin having had cancer. A maternal aunt also suffered from the same disease.

Hoarseness began in 1907-1908. This consisted of a slight huskiness which increased gradually until 1910, when he had almost complete loss of voice. He received no treatment until 1910. Patient then went to a specialist who made a diagnosis of laryngitis with some œdema of vocal cords. He took treatments occasionally until November 1, 1912, when he consulted Dr. E. H. Griffin, who made a diagnosis of epithelioma. Was also seen by Drs. Chisholm, Coakley and Bosworth, who confirmed the above diagnosis. Dr. Coakley removed a specimen which disclosed malignancy. While the diagnosis was being determined, potassium iodide was given in forty-grain doses three times a day for four weeks, in spite of a negative Wassermann reaction. No improvement followed.

*Operation* (December 31, 1912, by Dr. Stewart).—Tracheotomy under local anæsthesia followed by general anæsthesia through tube, and right vocal cord with tumor removed. The patient had difficulty in swallowing fluids for some time and was compelled to drink with neck lower than chest. Tracheotomy tube was removed at end of fourth week.

About March 15, 1913, he began to have difficulty in breathing again and returned to New York. Because of increasing difficulty in breathing, a tracheotomy tube was inserted about April 15, 1913. Examination of larynx disclosed almost complete stenosis. Examination of specimen removed through tracheotomy tube showed the histology of granulation tissue.

In July, 1913, because of the stenosis, the larynx having filled with either granulation tissue or new growth, the patient was referred to Dr. Howard Kelly of Baltimore, who gave two intralaryngeal and two extralaryngeal treatments with radium from July 18 to 27, 1913. After the first treatment there was a profuse discharge from throat, and on July 27 he was able to get air through larynx. On July 28, respiration through larynx was



GEORGE DAVID STEWART

fairly free and he has been breathing through larynx ever since. He has taken radium treatments on the following dates: September 18 and 19, 1913, intralaryngeal treatment for two hours and extralaryngeal treatment with six hundred and fifty milligrammes for fourteen hours, the last treatment being January 11, 1914, with eight hundred and two milligrammes.

Though he wears a tracheotomy tube, it has been plugged since the fall of 1913. Patient has seen Dr. Kelly twice since, but has received no further treatment.

Present condition: Voice hoarse, breathing free.

CASE III.—R. K., aged seventy years, married, German broker.

*Family History.*—Negative.

*Past Personal History.*—Patient has been a singer during entire life. Exercised voice daily. For many years was broker on floor of Stock Exchange, where voice was subjected to prolonged strains. Has smoked 2 or 3 cigars daily.

In 1908 he noticed a roughness in voice when delivering a short address. On one occasion during the same year after singing a difficult work, he experienced a sharp, knife-like pain in the larynx. Because of increasing roughness in voice, he consulted a throat specialist, who treated him for about a year and, in May, 1910, removed from the right vocal cord a papilloma. Following this he resumed his singing with no discomfort and greater success. After six months he became aware that his throat was not normal and gave up singing. The roughness in the voice reappeared and a specimen removed about November 1, 1914, proved to be malignant. He suffered no pain, no bleeding, no coughing, no difficulty in breathing. His only symptom was hoarseness.

*Operation* (November 11, 1914).—Tracheotomy under chloroform preceded by morphine. Anæsthesia continued through tracheotomy tube. Thyroid opened. Mass very distinct, involving and below true vocal cord on right, slightly across anterior commissure. Portion on left removed first; then that on right was trimmed off, dissecting it with curved scissors and a small periosteal elevator. Cartilage and upper part of wound closed. Tracheotomy tube left in.

*Remarks.*—Anæsthesia was very satisfactory.

*Pathological Report.*—Specimen consists of a small piece of tissue taken from surface of larynx below vocal cords. Microscopically, sections show a typical downward growth of squamous epithelium with "pearl formation." Diagnosis: Epithelioma.

Examined by Dr. Coakley May 7, 1915, who reported no evidence of a recurrence. At present writing, exactly one year after date of operation, there is no return of growth.







# THE RELATION OF GASTROSTOMY TO INOPERABLE CARCINOMA OF THE ESOPHAGUS

WITH A DESCRIPTION OF A NEW METHOD OF PERFORMING  
GASTROSTOMY \*

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Many surgeons never perform gastrostomy for the relief of malignant stenosis of the esophagus on the ground that it rarely prolongs the lives of patients in a satisfactory manner and contributes little to their comfort. The artificial feeding through the abdominal wall, even if the patients are permitted to chew their own food, is viewed as so unnatural and disgusting that the increased length of life secured thereby is not considered desirable. In my experience, a larger number of physicians and surgeons advise postponing a gastrostomy until it becomes impossible for the patient to swallow solid food any longer. In general, every attempt is made to postpone gastrostomy as long as possible.

Experience with gastrostomy, however, by those who have had opportunity to study the postoperative history of patients properly selected has proved that it does prolong life, and for a long time in many patients contributes considerably to their comfort. But experience also demonstrates that, in order to secure the best results from gastrostomy, it should be done early, not postponed until the very last minute, as is too often the custom. It is a mistake to allow these patients to become emaciated from inanition. If they are allowed to become thus weakened, it is often impossible to build them up again through the aid of a gastrostomy, or to enable them to survive the cancer for so long a time as if the operation had been performed earlier. It often happens

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\* From the Laboratory of Experimental Surgery, New York University and Bellevue Hospital Medical College.

that the course of malignant disease of the esophagus is favorably influenced by the rest afforded by relief from the stretching caused by deglutition. It has frequently been noticed that a carcinomatous esophagus has again become pervious after the rest afforded by a gastrostomy.

Among the objections urged against early gastrostomy are the considerations that the opening may leak; that the new fistula which leads to the stomach is permanently lined with granulation tissue and hence occasions some discharge; that from both these causes there may be some irritation of the skin in the neighborhood of the opening and, finally, that the necessity for the constant wearing of a tube is annoying. The early performance of a gastrostomy does not, of course, mean that the patient is placed immediately on catheter life, provided the above objections can be met. As long as the natural opening remains pervious to fluids, liquid can be taken by the mouth whether the gastric fistula is present or not, and the natural opening doubtless remains pervious longer with than without a gastrostomy opening.

The most serious of the objections to an early gastrostomy is the danger of leakage. Certainly, if the artificial fistula leaks, the excoriation of the skin from the contents of the stomach is considerable and is very distressing.

A number of methods, therefore, have been devised in order to prevent this contingency. That of Witzel,<sup>1</sup> has proved frequently unsuccessful. The method of Frank<sup>2</sup> is also often unsuccessful and very wasteful of the stomach-wall. In fact, with a small contracted stomach it is impossible to perform this operation. The method of Senn,<sup>3</sup> however, has proved successful in the hands of a number of surgeons. Moynihan and Robson consider it the best method, and recently Senn has collected reports of ninety-three cases of gastrostomy performed by this method in which leakage occurred in only two cases. The principle of the Senn method consists in the formation of a cone-shaped circular valve protruding into the cavity of the stomach and formed by reduplication of the stomach-wall around a tube introduced into the cavity of the stomach, the base of the cone being sutured to the parietal peritoneum. The

1. Witzel: *Centralbl. f. Chir.*, 1891, xviii, 601.

2. Frank: *Wien klin. Wchnschr.*, 1893, vi, 231.

3. Senn, Emanuel J.: *Gastrostomy by a Circular Valve Method*, THE JOURNAL A. M. A., Nov. 28, 1896, p. 1142.

crater of the cone then comes together around the tube within the stomach and prevents leakage. Kader<sup>4</sup> had modified this method by forming two lateral lips projecting into the stomach instead of a cone. This method, however, is not so serviceable in that it is more wasteful of the stomach-wall. As regards the prevention of leakage, the Senn method, therefore, may be considered as the most satisfactory method of gastrostomy hitherto published. In all operations in which artificial valves are formed, however, there is a tendency for the valves to diminish in size and effectiveness as time advances. This objection, probably, could not be urged against the Senn method when the operation is performed for the relief of carcinoma of the esophagus, as the valve doubtless remains efficient as long as there is any need for it. It might, however, become an objection in patients in whom it would be necessary to establish a permanent gastrostomy opening, as in a patient who might be expected to live indefinitely. Such permanent fistulas are sometimes, though rarely at present, indicated.

The establishment of a permanent fistula necessitates providing the fistulous tract with an epithelial lining. Without such lining two disadvantages, already cited, are present. The first is the constant presence of some discharge from the granulating tissue forming the fistulous tract. The second is the necessity for always wearing the gastrostomy tube. Perhaps the necessity for keeping the catheter in place may not exist in all cases, but in my experience it has seemed to be necessary and others have found it so and commented especially on it.

The creation of a gastric fistula which will not leak and which is lined throughout with epithelium and which, therefore, will neither discharge nor spontaneously close, appears to me to offer decided advantages. Such a fistula communicates with the skin surface with a meatus-like orifice and can be used or not as the patient wishes. It causes absolutely no inconvenience, and consequently can afford no reasonable argument against its early establishment in malignant disease of the esophagus.

The creation of such a fistula leading to the stomach is readily accomplished by a method which I have developed in dogs in connection with experimental removal

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4. Kader: *Centralbl. f. Chir.*, 1896, xxiii, No. 27, p. 665.



of the entire esophagus. The fistula has worked so well in dogs, not leaking even during vomiting or barking, that I have used the same technic with equal success on five human beings during the past year. The operation is similar to De Page's<sup>5</sup> gastrostomy, with which I was unfamiliar at the time of the experimental development of my own procedure. Whether the operation to be described be viewed as merely a modification of De Page's method or as sufficiently different to warrant its being designated as a new procedure, matters little. It is of importance only to call attention to the principle as the most desirable one for the establishment of a permanent gastric fistula.

The operation may be performed under local anesthesia and requires an incision of only 3 cm.

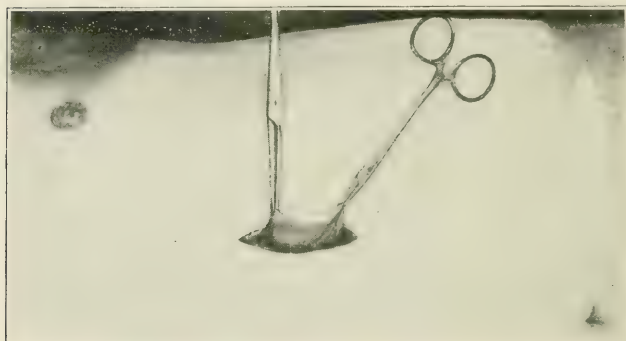


Fig. 1.—Nipple of anterior wall of stomach delivered through abdominal incision. Line of dashes indicates line of incision.

This incision is made parallel with the rectus fibers, over the inner third of the left rectus muscle a short distance (3 or 4 cm.) below the costal cartilage. The fibers of the rectus are not divided, but separated bluntly. Its posterior sheath is divided and the peritoneal cavity entered. The anterior wall of the stomach is now pulled out through the wound. This nipple of stomach-wall is then held to the left by two clamps (Fig. 1).

An incision from 3 to 4 cm. long is then made between the two clamps. Two short perpendicular incisions 1 cm. long, extending toward the greater

5. Jour. de Chir., 1901-1902, i, 715.

curvature, are then made at each extremity of the first cut. The flap *C E G F* created by these incisions, *F G*, is then folded over to the left and *A* is pulled down to the right. By this procedure the opposite margins indicated by the letters *F C B A* and *G E D A* are approximated, and when sewed together form a tubular canal (Fig. 3). In this manner a long canal is created in the stomach-wall, at least 5 cm. long, without diminishing the transverse diameter of the stomach.

Near its base this canal is then sutured to the parietal peritoneum and to the posterior sheath of the rectus. Its apex end is sutured to the skin of the abdominal wall. The operation is a less extensive plastic procedure than that devised by De Page. It can easily be per-

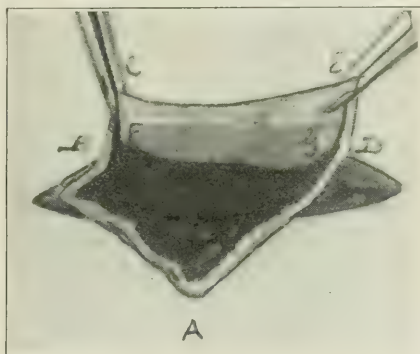


Fig. 2.—Opening into the stomach made by the incisions through the stomach-wall.

formed on a small nipple of stomach-wall delivered through a very short incision. Much less of the stomach-wall is used up in the creation of the new canal than in De Page's operation. Moreover, in the above-described method the suture-line is placed on the upper surface of the tubular canal, thus subjecting it to less strain from the weight of the filled stomach. Furthermore, the small plastic flap receives its blood-supply from the greater curvature. This consideration is of greater importance, if there are metastases of the lymph-nodes in the lesser omentum. The formation of such a canal in no appreciable way alters the shape of the stomach. Instead of being narrow or constricted at the region

from which the new canal is made, the stomach contour is unchanged.

De Page's operation has been described by Robson as a complicated procedure, but certainly the steps of the smaller operation which have been here outlined are not complicated and can be performed on a very small portion of the stomach-wall with the aid of local anesthesia alone.

The operation results in the formation of a long canal from three to four times the length of the two short incisions at the extremities of the first cut. As already mentioned, the effect is to cause the stomach-wall, at the place where the tubular canal is formed, to lengthen out

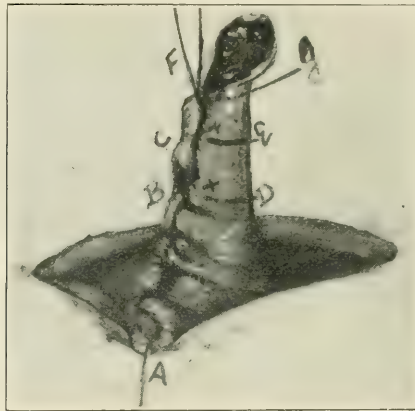


Fig. 3.—New canal, tubular in shape, formed by after-suture of plastic procedure shown in Figure 2.

in a surprising manner. The split rectus fibers come together around this canal and act like a sphincter.

The anchoring of the new canal in place may be accomplished in two ways: either the base of the new canal may be sutured to the margin of the rectus sheath, as previously explained, or the inner extremity of the canal may be inverted a short distance into the cavity of the stomach. By this procedure a circular valve is created, as in the Senn method of gastrostomy. Although the addition of this valve furnishes an increased safeguard against leakage, it may be omitted and good after-results obtained. Of much more importance than the creation of a circular valve at the inner extremity of the

new canal, in fact the essential feature of this operation, is the direction given to the new canal by the selection of an area of the stomach-wall for the performance of this plastic procedure somewhat to the right of the abdominal incision. The new canal, when formed, should have an oblique direction to the left. Any increase of intragastric pressure will then bring the walls of the fistula together and effectually prevent the escape of stomach contents.

I have performed gastrostomy five times as detailed above and always without inverting the proximal end of the new canal. In other words, in five patients I have simply sewed the new canal near its base to the margin of the opening in the rectus sheath and the mucous membrane of the external opening of the canal to the skin, depending entirely on the constricting influence of the rectus fibers and the oblique direction of the new canal for tight closure. In three of these patients the malignant disease was so far advanced that they did not survive the operation long enough (three or four weeks) to be up and around, and there was no opportunity, therefore, to test the tightness of the new canal in a satisfactory manner. These three patients occupied a recumbent position all of the time after operation. There was not a drop of leakage in any of them. Of the two other patients, one lived a sufficient length of time after the gastrostomy to be up and around as a normal individual, and he had no leakage. The fifth patient is still living. He has had leakage only on severe exertion. Such leakage, however, has been inconsiderable and the patient has been in the habit of controlling it by inserting a soft rubber stem pessary when going to work (he is a carpenter). For the past three months he has been unable to work and has omitted the use of the pessary altogether.

104 East Fortieth Street.

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## GASTROSCOPY \*

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NEW YORK

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It is unnecessary, in a paper attempting to enlist interest in gastroscopy, to emphasize the frequency of cancer of the stomach and how rarely this disease is diagnosed in an early stage. Only one question presents itself for discussion. Is gastroscopy an efficient and practical method of viewing the interior of the stomach? By an efficient method is meant one which permits the details of the mucous membrane of a sufficient portion of the stomach to be seen clearly. By a practical method is meant one which is not dangerous and does not entail too much inconvenience or suffering on the part of the patient, and, perhaps, one which furnishes more information than other existing methods of objective examination.

No one, for instance, would question the value of inspecting the interior of the stomach or the obligation which rested on the physician of insisting that patients with new gastric symptoms should submit to an examination of this character if he believed that the procedure was really efficient and practical in the sense just defined.

It is the object of this paper and the demonstration accompanying it to show to the members of this Section how much of the interior of the stomach can be seen, how clearly it can be seen and with what little inconvenience in the normally formed person.

It is true that the patient selected for this demonstration is a favorable subject; nevertheless, he illustrates none the less truly what can be accomplished in the average patient, though not always under local anesthesia.

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\* Read in the Section on Practice of Medicine of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

\* From the Department of Experimental Surgery of New York University and Bellevue Hospital Medical College.

Although I believe that anyone who witnesses this demonstration would be forced to admit that on this patient, at least, gastroscopy is an efficient and practical method of viewing the interior of the stomach, the fact nevertheless remains that for more than thirty years numerous attempts have been made to improve the technic of gastroscopy without gaining for this method of examination even a small part of that recognition which cystoscopy has acquired. This consideration naturally reflects some doubt on any claim to improvement which would place gastroscopy on a new plane of efficiency.

Figure 1 represents the cardiac sphincter. Figures 2 and 3 represent the entrance to the pyloric region of the stomach at the place of transition from the vertical portion of the stomach to the horizontal portion. Figure 4 represents a view in the opposite direction toward the

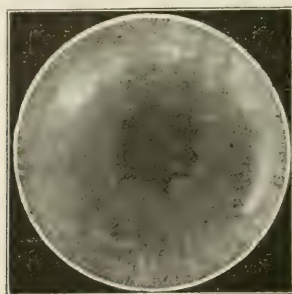


Fig. 1.—Cardiac sphincter—direct view

fundus or cardiac region. It illustrates the anterior and posterior walls of the stomach separated by a central cleft-like cavity. Figures 2, 3 and 4 are seen through an indirect telescope viewing the mucous membrane at right angles to the direction of the instrument. Figure 5 represents the stomach in the direction of the greater curvature viewed directly. It must be quite evident to anyone that, if views of such a degree of clearness can be obtained within the stomach, the method of examination is not only of positive, but also of negative diagnostic value. The character of these views depends alone on efficient illumination. I have tried four other types of telescopes, but have been unable to obtain the satisfactory view of the interior of the stomach here demon-

strated until I had constructed the lamp and lens system of the instrument used in this demonstration. The lamp is as large as the caliber of the sheath of the instrument and furnishes sufficient light to illuminate the whole of the distended stomach.

The use of so large a lamp is made possible by the device for pressing it to one side after it has been introduced into the stomach. I have compared its degree of

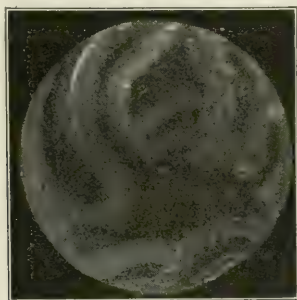


Fig. 2.—Entrance to the pyloric region of the stomach at the place of transition from the vertical to the horizontal portion—indirect view.

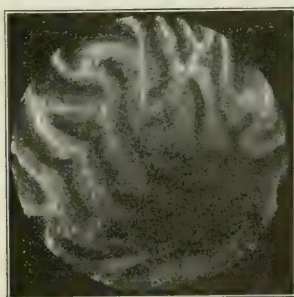


Fig. 3.—Entrance to the pyloric region of the stomach at the place of transition from the vertical to the horizontal portion—indirect view.

illumination and the views possible by it with those obtained by the indirect type of instruments made on the plan of the indirect cystoscopes and am convinced that the latter type of instrument will not enable one to see distinctly within the stomach. The lens system does not afford a view through a wide angle, but enables the eye to see clearly up to within 4 inches from its surface.

When suspicious appearances are found the direct view telescope may be focused on the area, as illustrated in Figure 5, and a piece removed for microscopic examination. Up to the present I have made a positive diagnosis by one or the other of these methods in twenty cases of cancer of the stomach. The roentgenoscopic examination was negative in two of these cases. The field of usefulness of the Roentgen examination of the stomach and of gastroscopy are not quite the same. But the two methods complete each other well. Roentgenoscopy furnishes accurate information regarding the condition of the pylorus. This is, of course, the most important region of the stomach in which the largest number of ulcers and carcinomas originate. On the other hand, gastros-

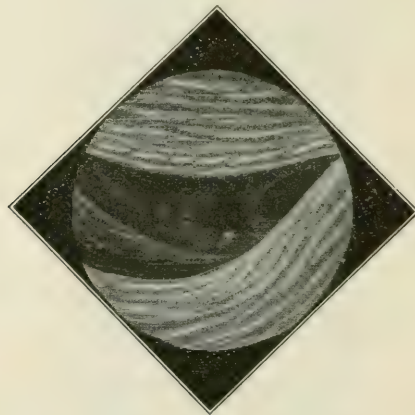


Fig. 4.—View toward the fundus or cardiac region—indirect view.

copy furnishes exact information, both positive and negative, about the condition of the vertical portion of the stomach. This includes by far the largest portion of the stomach and the region of the lesser curvature, but not the region, perhaps, in which the majority of ulcers and cancers originate. It does, however, include a region occupied by a large proportion of cancers and those which are particularly difficult to recognize clinically or by any other method of objective examination, even including Roentgen cinematography. One can, therefore, see inside the stomach with a degree of clearness which completes in a needed manner other existing objective meth-

ods of examination. It is possible, moreover, in the normally formed person, to make the examination without undue discomfort and with safety.

I am convinced that, if proper gentleness and carefulness of technic are exercised, it is possible to diagnose cancer of the cardia simply with the aid of cocaine-ization of the pharynx and without causing pain or an amount of discomfort to which a normal person would object.

Some discomfort, except in rare persons, like the one who has lent himself for this demonstration, is experienced and the nervous apprehension of the average patient at the thought of having a rigid instrument inserted into the stomach is such that I have concluded that the examination in a large percentage of patients

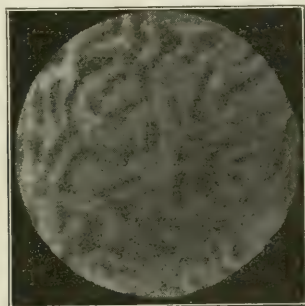


Fig. 5.—The stomach in the direction of the greater curvature, viewed directly.

is more satisfactorily conducted under a general anesthetic. For this purpose we have in intratracheal anesthesia, a new method which makes possible in gastroscopy that which previously has not been possible. For gastroscopy it is superior to intravenous or rectal anesthesia because it prevents any obstruction to the elimination of the ether which may be caused by pressure of the gastroscope on the trachea. It is possible, moreover, to conduct the whole examination after the administration of a small amount of ether under nitrous oxid and oxygen by a method perfected for this purpose and about to be described. I believe that the possibility of conducting gastroscopy under nitrous oxid and oxygen anesthesia introduces a new considera-



tion in gastroscopy which, if it proves uniformly successful, will remove the last objection to the routine use of this method of examination on the ground of discomfort to the patient. Certainly, if it is possible to examine the interior of the stomach in a patient anesthetized with an anesthetic associated with so few unpleasant after-effects as those which follow nitrous oxid anesthesia, there should be no objection to the routine application of a gastroscopic examination when what it reveals may mean so much to the patient.

As regards the safety of gastroscopy, are there any dangers connected with passing a rigid tube into the stomach? Dr. Chevalier Jackson long ago proved that the procedure is devoid of danger; and how can it be otherwise if the eye of the observer is always kept on the distal end of the instrument? If the end of an instrument which is inserted into the esophagus and then into the stomach is never allowed to progress except where the folds of mucous membrane fall away before it by air distention in its passage down the esophagus, how can any injurious trauma be caused? Except in the case of one patient at the very beginning of the work when my technic was faulty, I have never had any unpleasant consequences.

The late diagnosis of gastric cancer, particularly of cardiac cancer, has long been a blot on the reputation of medicine. I believe that we now have two methods, Roentgen cinematography and gastroscopy, which do not cover the same field, but which complement each other, and by which it is possible to make the diagnosis of carcinoma of the stomach when the presence of this disease is suspected. It is no longer a question of inability to make the diagnosis, but, in the words of Dr. Jackson, of "looking and seeing."

It may perhaps be a question of the patient's complaining of symptoms early enough, but if gastroscopy and roentgenoscopy are made a routine in cases in which the diagnosis of cancer is among the possibilities, a large proportion of carcinomas of the stomach will be found in a stage in which it is possible to do something for them. Of not less importance, perhaps, is the consideration that we shall be discharging an obligation which we owe these patients.

It is surely desirable to be in possession of the information afforded by these two methods of examination before resorting to exploratory incision. If this rule is followed the exploratory operation may prove unnecessary, or, if this is indicated, the surgeon will be in a better position to proceed with a radical operation.

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INTRA-TRACHEAL ANESTHESIA FROM THE STAND-  
POINT OF THE NOSE, THROAT AND ORAL SUR-  
GEON WITH A DESCRIPTION OF A NEW  
INSTRUMENT FOR CATHETERIZING  
THE TRACHEA.

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DR. HENRY H. JANEWAY, NEW YORK CITY.

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(Reprint from *The Laryngoscope*, St. Louis, November, 1913.)





# **INTRA-TRACHEAL ANESTHESIA FROM THE STANDPOINT OF THE NOSE, THROAT AND ORAL SURGEON WITH A DESCRIPTION OF A NEW INSTRUMENT FOR CATHETERIZING THE TRACHEA.\***

**DR. HENRY H. JANEWAY, NEW YORK CITY.**

The satisfactory manner in which intra-tracheal anesthesia for operations in the nasal, oral or laryngeal regions or even within the trachea or bronchi meets the requirements demanded during such operations is deserving of special comment. The very multiplicity of methods of administering an anesthetic during nose and throat operations testifies to the presence of dissatisfaction with most of the methods in common use. This dissatisfaction is most apparent in the usual methods of anesthesia in which the anesthetic is inhaled from a cone. Under such conditions the surgeon can operate only during the intervals when the cone is removed. The anesthesia can never be a smooth one, but is characterized by periods of more or less profound coma alternating with periods of partial return to consciousness. During the latter, there is often more or less struggling and, perhaps, coughing or retching. Often the operation must be discontinued at very critical periods, at times for instance, when the hemorrhage may not be entirely controlled. Operating under such conditions greatly increases the dangers and risks, and unnecessarily prolongs the operation. The difficulty of preventing the inhalation of blood and mucus is great, and constant care and attention is necessary in order to prevent such a complication. When the patients are profoundly anesthetized asphyxia from the falling back of the tongue is frequently troublesome. Lane of London, who formerly used this method in connection with his cleft palate operations, has well remarked that anesthesia for oral operations demands the services of an expert anesthetist and one, preferably, who is accustomed to work with the operator.

A more useful method is intra-nasal or pharyngeal anesthesia. By this method the ether vapor may be conveyed to the patient through glass bulbs fitted into the anterior nares or by means of a catheter passing to the pharynx through the nose. Both these methods are much more satisfactory than the preceding. Their use permits of

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\*From the Department of Experimental Surgery of New York University and Bellevue Hospital Medical College.

a more even anesthesia and, especially when the catheter is used through the nose, of a much greater ease in preventing inhalation of mucous or blood. Neither method, however, is entirely satisfactory in this last respect. The blood and mucus within the mouth must be constantly sponged or sucked out, the head must be kept well thrown back and frequently trouble is experienced because of the falling back of the tongue.

Many surgeons have resorted to rectal anesthesia in order to avoid the inconvenience of the proximity of the anesthetist and his apparatus during operation about the head. Rectal anesthesia, however, has never come into general use. Perhaps this is an unfair argument to use against it. Its administration, nevertheless, requires considerable skill and accurate dosage by it is somewhat

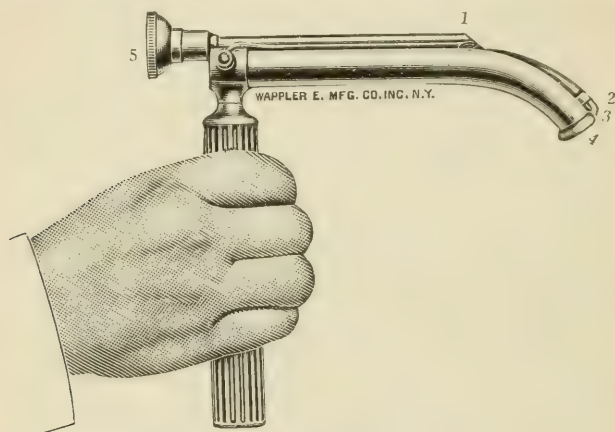


Figure 1. Indirect speculum for catheterizing the trachea. 1. Prism. 2. Lamp. 5. Objective glass through which the eye of the observer views the larynx in the direction of 3-4.

difficult. The rectum also must be carefully cleaned beforehand. Under usual conditions and with expert care irritation of the rectum is rarely produced. Cunningham, Leggett and Sutton have laid down the principles and developed the technic to a high point of efficiency.

Intra-venous anesthesia, only recently experimented with in this country, fulfills somewhat the same indications as rectal anesthesia.

To Dr. Francis Honan belongs much of the credit for developing in this country a successful technic for the administration of intra-venous anesthesia.

With both rectal and intravenous anesthesia the surgeon must rely entirely upon the patient's position in order to protect the

trachea from the inhalation of blood and mucus and it is absolutely important to provide for free expiration in order to regularly eliminate the ether.

In contrast, however, to all these methods, anesthesia by intra-tracheal insufflation, i. e. through a tube introduced into the trachea, meets the requirements of the nose, throat and oral surgeon in an eminently satisfactory manner. Either ether or nitrous oxid and oxygen may be used as the anesthetic. With a minimum of effort on the part of the anesthetist, a perfectly even anesthesia is produced with complete relaxation of the patient and the maintenance of a rosy color. This statement is as true of nitrous oxid and oxygen, assuming that the patient is a normal individual, as it is of ether. In fact intra-tracheal anesthetization by both ether and

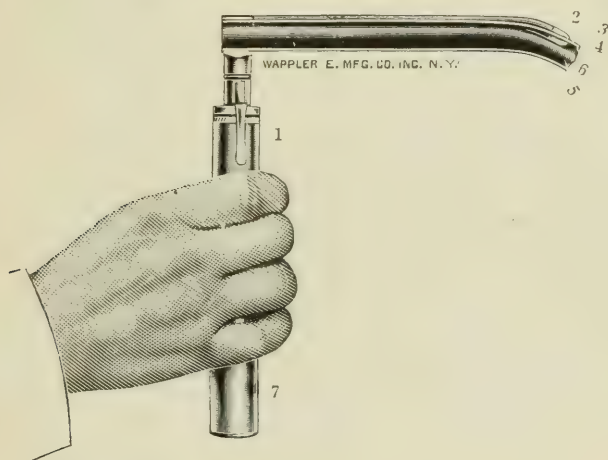


Figure 2. Direct speculum for catheterizing the trachea. 1. Press button for illuminating the lamp. 2. Lamp. 3-4. Direction of vision. 5-6. Direction taken by the catheter. 7. Handle containing two dry cells.

nitrous oxid renders possible a better and more complete anesthesia that can be obtained by either of these anesthetics when administered in the ordinary manner. It is, therefore, questionable whether intra-tracheal anesthesia should not be used very generally.

The only drawback to intra-tracheal anesthesia is the difficulty sometimes experienced in inserting the intra-tracheal catheter. To the expert laryngologist it may seem that catheterization of the trachea should always be a simple matter. In the fully relaxed patient it is frequently an easy matter to pass a rubber catheter into the trachea with the fingers alone. In many patients, fully relaxed, the larynx can be seen and catheterized without even flex-

ing the head by the aid of the Jackson direct laryngoscope after the manner described by Dr. Richard Johnston of Baltimore.

The most reliable method of all is by means of the Jackson direct laryngoscope with the head in extreme extension. Even if simpler methods were as uniformly successful, the use of the direct laryngoscope in this manner would be preferable for the very important

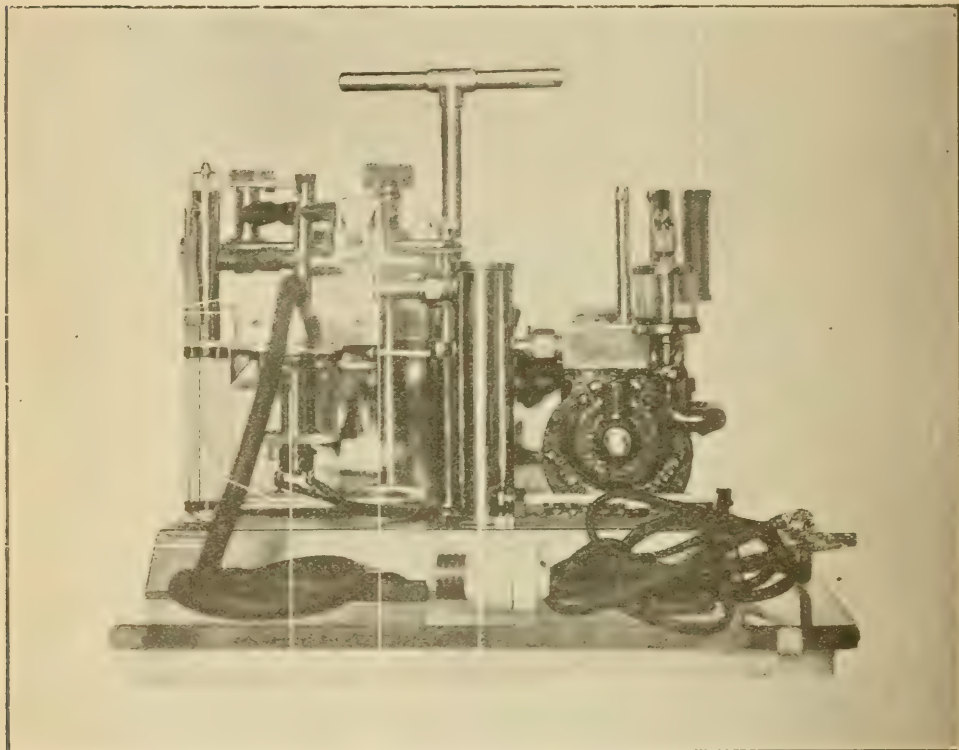


Figure 3. Apparatus for administering intra-tracheal ether anesthesia. It measures 12x14 inches and weighs 28 pounds. 1. Rotary blower; 2. Over the position of the motor which is hidden behind the ether jar. 3. Air filter and muffler into which the air passes from the blower. 4. Slide valve through which the air passes from the filter. It shunts any desired portion of the air from passing through the ether jar. 5. Ether jar. 6. Water jar, containing an electric heater for warming and moistening the current of air. 7. Interrupting slide valve operated by a worm wheel in the position indicated by the arrow "9," but hidden in the picture behind the blower "1." 8. Air pressure safety valve which can be set to blow off at any desired pressure. 10. Manometer. 11. Rubber tube conducting the air to the patient.

reason that it permits of inspection of the larynx before the insertion of the catheter. Dr. Chevalier Jackson has called the writer's attention to one death already attributable to intra-tracheal anesthesia because of failure to previously inspect the larynx.

Not a little trouble has been experienced, however, in the intro-



duction of the intra-tracheal catheter by this method. In fact, Dr. Connell of Roosevelt Hospital, whose experience has been very large, expressly states, (*Surgery, Gynecology and Obstetrics*, August, 1913, p. 50), that although intra-tracheal anesthesia is the best form of anesthesia and always superior to pharyngeal anesthesia, yet the difficulty of catheterizing the trachea will always prevent

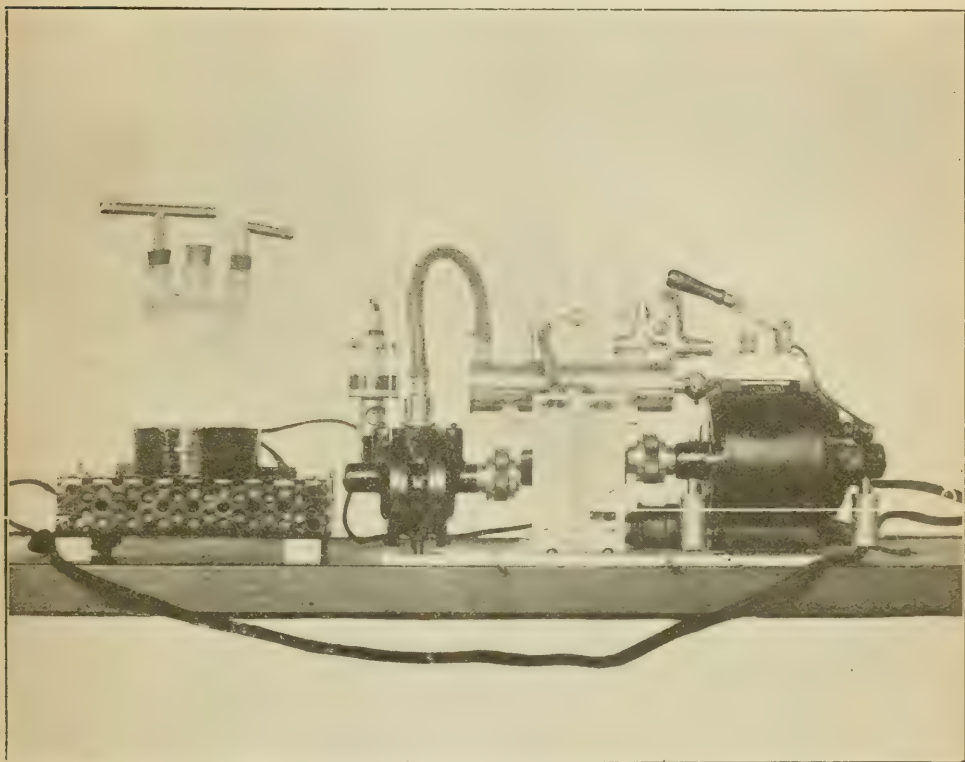


Figure 4. Apparatus for intra-tracheal anesthesia capable of being carried in small hand-bag. It measures  $4\frac{1}{2}$ "x5"x15" and weighs 18 pounds. 1. Motor. 2. Blower. 3. Slide valve controlling the proportion of air passed over the ether. 4. Filter. 5. Safety valve. 6. Ether flask. 7. Rheostat. 8. Manometer.

the general adoption of the method. The writer's own experience confirms this view. He has seen another surgeon, who has administered as many as 500 intra-tracheal anesthetics, waste no little time in attempting to introduce a catheter into the trachea.

It will be unfortunate if a method of anesthesia so universally successful and valuable as intra-tracheal anesthesia fails to receive general adoption because of these difficulties. The main trouble in catheterizing the trachea is the tendency for the catheter to fall



back into the esophagus. In using the direct laryngeal speculum the writer has frequently been impressed with the great advantage which would be offered by some means which would bend the distal end of the catheter forwards, if only a little forwards, so as it passes over the distal end of the direct laryngoscope. A wire stylet accomplishes this but is inconvenient to use.

In order to accomplish it in a simple manner, the writer has devised the speculum represented in Figure 1. It in part meets con-

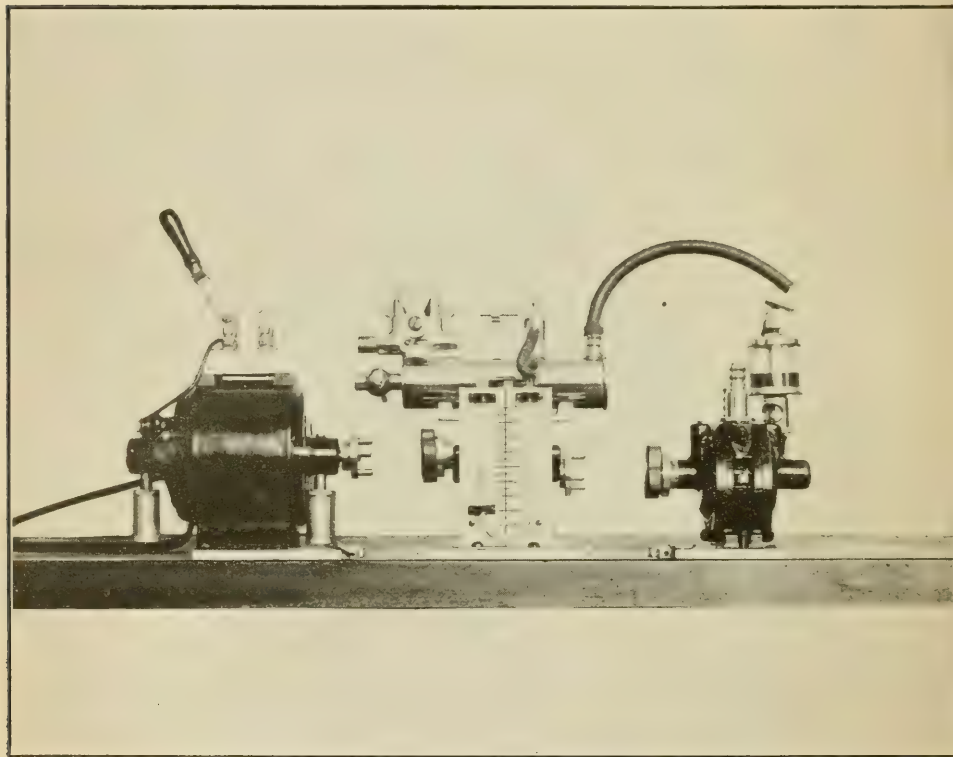


Figure 5 illustrates the manner in which the smaller apparatus may be taken apart into three pieces.

ditions demanded. At "1" is a prism which permits of visions in the direction 3-4 when the eye of the observer is placed at 5. With this instrument catheterization of the larynx after cocainization of the pharynx is an exceedingly simple matter in both the conscious and anesthetized patient and with but little extension of the head.

It has been discovered, however, that by shortening the distal end of this speculum the larynx may be viewed directly, that is, without the aid of the telescope, just beneath the distal termination of the

curved upper half of the speculum and through its central notch which serves to keep the catheter in the middle line, Figure "2."

This control of the distal end of the catheter even though it causes only a slight forward bend of the catheter offers a very great advantage. It permits of easy catheterization of the larynx even when the patient's pharyngeal reflexes are not completely abolished and without the necessity for the same degree of extension of the head. The omission of the telescope greatly simplifies the instrument, while the possibility of viewing the larynx directly is superior to viewing it indirectly, even though the latter method permits of a greater curve in the distal end of the catheter.

The illumination is obtained through a lamp placed at "2," which is lighted through two small storage cells contained in the handle of the instrument.

With this instrument, a large size of catheter  $\frac{3}{8}$  of an inch in diameter designed for intra-tracheal anesthesia by nitrous oxid and oxygen may easily be introduced into the larynx.

As soon as the tube has been introduced its external extremity is connected with the tube from the insufflation apparatus; and from this time on, that is before the beginning of the operation, the anesthetist may take his position at any convenient distance from the patient and the operator is unhindered by his presence or by an anesthetizing apparatus other than the tube emerging from between the patient's teeth. This tube, for mouth operations, is best held in place by an assistant who also manages the mouth-gag and retractors, for then it may be moved at will to any portion of the mouth not within the field of operation. For other operations, a small metal tube, one inch long, may be slipped over it between the teeth. This is kept from slipping out of the mouth by a spring which passes behind the neck somewhat in the same manner as a frame truss which maintains its position by pressure around the back. Figure 3 and 4 represents the author's apparatuses designed for supplying the ether vapor to the intra-tracheal tube. There are several features about them which deserve emphasis even at the expense of repetition. Figure 3 represents an apparatus which may be described as an easily portable machine, weighing about 28 pounds and measuring 10x12 inches and capable of supplying a continuous current of warm, moistened air saturated with any desired amount of ether vapor. The current may be interrupted automatically for the purpose of allowing regular deflation of the lungs.

These features are all of some importance and contribute to the best results in anesthesia. The temperature of the air delivered at

the end of a tube three feet long has been measured. It is 95 degrees, at least 15 to 30 degrees higher than a current of air coming directly from the ether bottle. It is also perceptibly moistened, and we are forced to believe that the every day experience of the evil effects of mouth-breathing makes it evident that warmed ether vapor mixed with moistened warm air approximate more closely to the normal physiological conditions and are better borne.

Next, concerning the amount of ether vapor. In the above apparatus it is possible to regulate the amount of ether in two ways, first by the slide valve "4" any portion of the current of air may be diverted from passing over the surface of the ether, second, by the cock handle "12" controlling the inlet valve to the ether flask, the percentage of ether vapor in the current of air may be increased over an amount which it is possible to pick up by simply passing the air over the surface of the ether by bubbling a portion of this air through the top layers of the ether. This additional quantity is sometimes needed with alcoholic patients.

Finally as regards the interruptions. By laboratory experiment there seems to be no change in the sphymographic tracings of the pulse produced by regularly interrupting the current of air supplied during intra-tracheal anesthesia when the anesthesia is administered within the limits of the proper pressures for intra-tracheal anesthesia. Very serious diminution of the volume output of the heart is produced by higher pressures. The greatest benefit obtained by interrupting the current of air is the effect of such interruptions when regularly and automatically performed upon respiration. The author possesses tracings which demonstrate the almost entire abolition of efforts at respiration caused by interrupting the current of air during intra-tracheal anesthesia. Such a condition renders the anesthesia far safer and does much, not only to conserve the expenditure of energy by the patient, but the ease of operating for the surgeon. In this apparatus only the physiological effect upon the patient is depended upon as the guide to the correct percentage of ether to use. Such is a safe guide, though Dr. Connell has rendered surgeons a service in defining the correct percentages and showing how closely definite percentages can be followed.

Figure 4 represents an apparatus which is still smaller and, therefore, more portable. It weighs only 18 lbs. and measures  $4\frac{1}{2} \times 5 \times 5$  inches. By removing the two pins penetrating the base plate the apparatus will come apart in three pieces as illustrated in Figure 5 and may then be packed in a small hand-bag. This smaller ap-

paratus is most simple in construction. It contains the same size blower and motor as the apparatus figured in Figure 3 and only differs from the latter in not running quite so noiselessly and in not being provided with so serviceable a means for interrupting and warming and moistening the current of air.

Actual trial with this apparatus during a period of eight months has given uniformly good results. In the majority of cases in which the writer has used the apparatus there have been some special indications for it. Five have been intra-thoracic cases and, in most of the other cases, the operations were within the nose, mouth or about the head. It has given all the advantages which have been claimed for intra-tracheal insufflation. The operations were conducted without interference from the anesthetist or his apparatus and the anesthesia was smooth and uninterrupted. On no occasion was there any inconvenience from blood or mucus in the throat. During the past two years the writer has made a considerable number of esophagoscopy and gastroscopy examinations. These he usually conducts under local anesthesia, but for a complete gastroscopic examination it is desirable to give a general anesthetic. The ease of making these examinations with the smooth uninterrupted anesthesia produced by the intra-tracheal anesthesia contrasted strongly with similar examinations conducted under anesthesia produced by inhalation through the mouth.

Bronchoscopic examinations and operations may similarly be performed under intra-tracheal anesthesia—a small catheter may be inserted by the side of the bronchoscopic tube, or the insufflation apparatus may be connected directly to the bronchoscopic tube and the ether vapor administered intermittently.

In fact, it is interesting to note that a number of years ago Dr. Chevalier Jackson availed himself of true intra-tracheal insufflation and at the suggestion of T. Drysdale Buchanan added an auxiliary ether tube to his bronchoscope.

In conclusion, for the longer operations of the nose, throat and oral surgeon, intra-tracheal anesthesia meets the indications in a manner that no other form of anesthesia does.

The technic of nitrous oxid and oxygen by intra-tracheal insufflation differs considerably from ether anesthesia and will be described in another communication.

104 East Fortieth Street.





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APRIL, 1914.

**SIMPLE AND COMPLETE FORMS OF APPARATUS  
FOR INTRATRACHEAL ANÆSTHESIA.\***

**BY HENRY H. JANEWAY, M.D.,**

OF NEW YORK.

(Published from the Department of Experimental Surgery of N. Y. University and Bellevue Hospital Medical College.)

IN the August number of the ANNALS OF SURGERY for 1912, an apparatus for the administration of intratracheal anæsthesia was described for which the advantages of compactness in size and ease of transportation were claimed.

Since that time the apparatus has been improved; both its weight and size have been materially diminished. Because of the useful field which intratracheal anæsthesia is destined to fill, improvements of these characters justify a brief description.

Fig. 1 represents an apparatus which is fitted with only those parts which are considered necessary for intratracheal anæsthesia. It weighs eighteen pounds and measures  $15 \times 4\frac{1}{2} \times 5$ . It may be taken apart into three pieces, by removing the pins in the base plate, and can be carried in a small handbag. It is provided with a safety valve and air filter.

Fig. 2 illustrates a machine designed for hospital work but easily portable. All the parts are attached to one base plate. In addition to safety valve, air filter, and ether jar, it contains provisions for warming and moistening the current of air and for automatically interrupting the same at desired intervals. It runs noiselessly and measures  $14 \times 10 \times 8$  inches and weighs 28 pounds.

Fig. 3 illustrates an apparatus containing all the parts mentioned in the description of the machine represented in Fig. 2, but in addition, provision for measuring accurately the current of air and percentage of ether vapor. All these parts are fixed upon one base plate. It weighs 35 pounds and measures  $19 \times 10 \times 8$  inches. Dr. Karl Connell has demonstrated the constancy with which definite ether percentages may be adhered to during anæsthesia. This work has been confirmed by Boothby, of Boston, and the author is convinced of the truth of these claims. Ether may, therefore, be administered with greater scientific accuracy and safety to patients when it is possible to accurately control the percentage given.

In this machine the varying quantities of ether are delivered to the vaporizing jar by a piston which can be set to deliver any desired quantity per minute. The quantity of air is measured by the height to

\* Read before the American Association of Anæsthetists, June 18, 1913.

which a float rises within a perpendicular tube, the lumen of which is shaped like a truncated cone. The higher, therefore, that the float rises the larger is the circular space around it and between it and the walls of the tube. This form of meter works accurately and may be tested at any time in the offices of any gas company.

We have tested it by a wet meter purchased for the purpose and have found no variations during a period of several months.

All these machines work on both the alternating and direct current.

When the author first used this machine he was not entirely assured that the administration of ether in known percentages offered a material advantage, especially if the services of an expert anæsthetist should be at hand. In whatever manner ether is administered, the physiological effect upon the patient is the only safe guide to the amount of ether which should be given. While it always is a satisfaction to know the amount of air and the percentage of ether which the air contains, this knowledge can only be obtained at the expense of adding to the apparatus extra parts for this purpose.

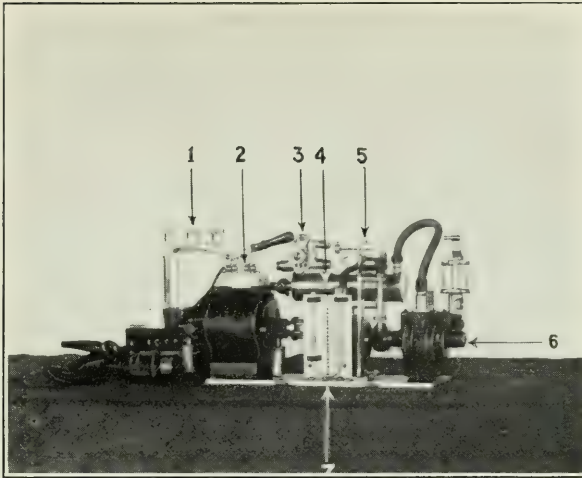
Continued use of the machine has convinced the author that a knowledge of both the amount of air and the quantity of ether administered per minute is more than a satisfaction. It prevents, on the one hand, inconveniences amounting sometimes to actual dangers from the use of improper quantities of air and renders possible the administration of ether with far greater accuracy.

The device for mechanically interrupting the current of air is to be viewed in the same light. Regularly interrupting the current of air makes no difference in the blood-pressure, when the current of air is supplied within the pressure limits which are indicated during intratracheal anæsthesia.

It is well to remember that at a high pressure, which sometimes may occur accidentally, the pulmonary circulation can be sufficiently compressed to reduce seriously the output of the heart and the general blood-pressure. This change is illustrated in Fig. 4.

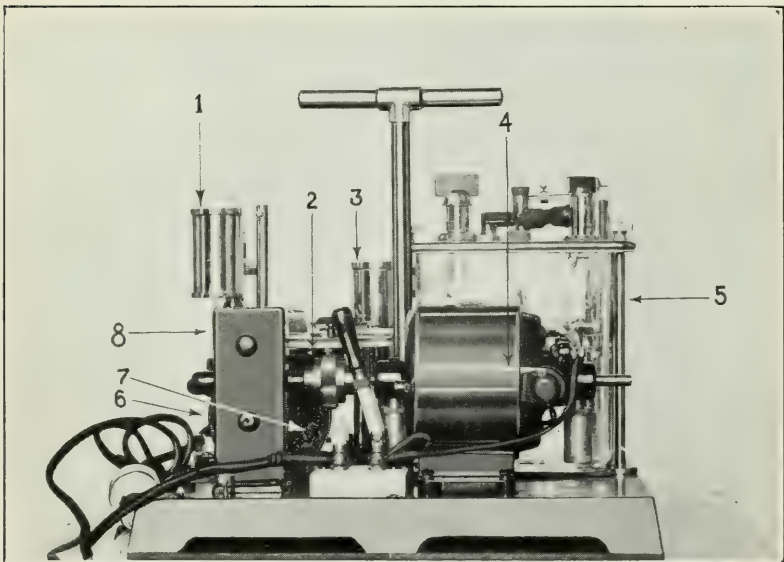
The great benefit from regularly interrupting the current of air is noticed during intrathoracic operation when the thorax has been opened. Fig. 5 illustrates the contrast during the same

FIG. 1.



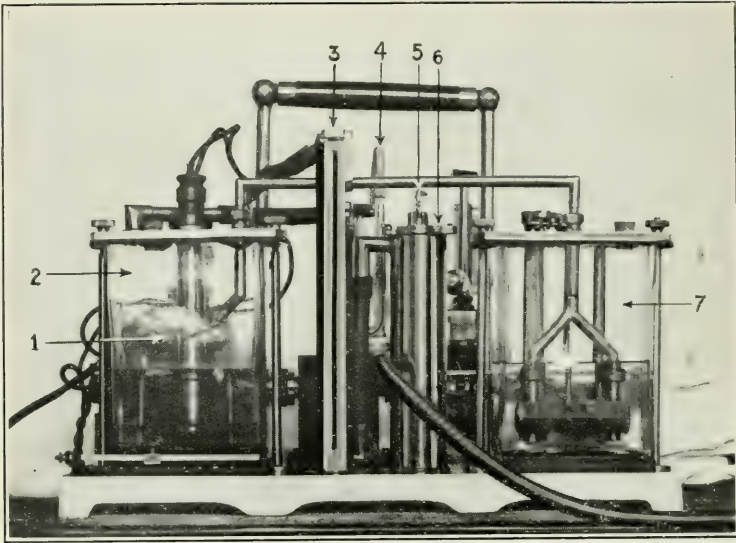
Smallest apparatus for intratracheal anæsthesia, measuring  $4\frac{1}{2} \times 5 \times 15$  inches and weighing 18 pounds. 1, ether flask; 2, motor; 3, slide valve controlling the percentage of ether administered; 4, air filter; 5, safety valve; 6, blower; 7, manometer.

FIG. 2.



Complete apparatus for intratracheal anæsthesia except for means for measuring ether percentages. Weighs 28 pounds and measures  $10 \times 14$  inches. 1, muffler and air filter to intake of blower; 2, worm wheel which operates the interrupter to the current of air; 3, second air filter between the blower and ether flask; 4, motor; 5, ether flask; 6 and 7, blower; 8, gear box.

FIG. 3.



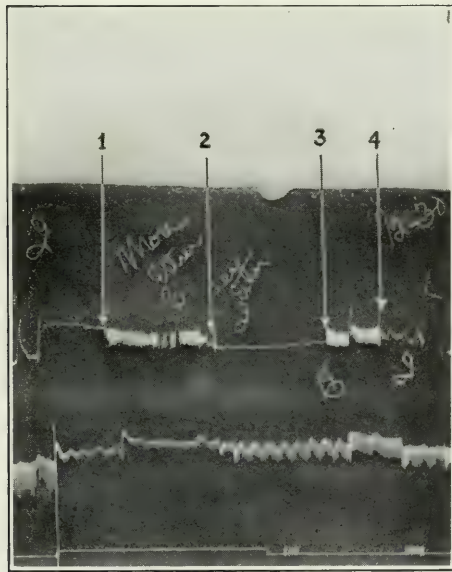
Apparatus for intratracheal anæsthesia with provisions for measuring ether percentages. Weighs 35 pounds and measures 19 x 10 x 8 inches. 1, motor seen through the volatilizing flask; 2, volatilizing and warming flask; 3, air meter; 4, manometer; 5, safety valve; 6, air filter; 7, ether flask

FIG. 4.



Showing diminution of blood-pressure and output per heartbeat when intrabronchial pressure was raised from 10 to 22 mm. Upper tracing measures the output per beat of the heart. Lower tracing measures the blood-pressure.

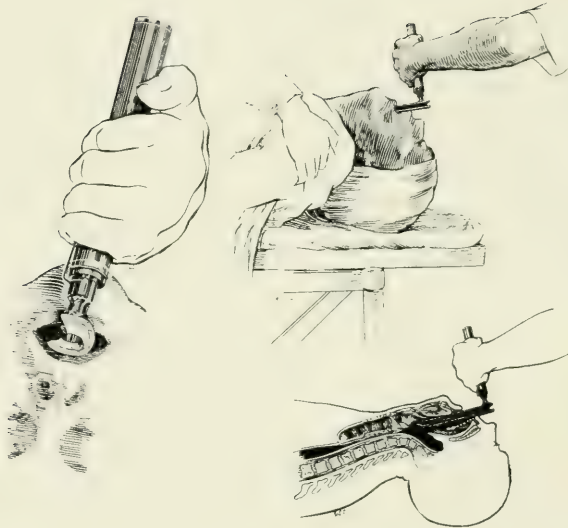
FIG. 5.



Illustrates effect upon respiration when the current of air is interrupted with the thoracic cavity open. Upper tracing, the respiration curve; lower tracing, the blood-pressure curve between 1 and 2, and between 3 and 4 the current of air was not interrupted,



FIG. 6.



Illustrating the position of the head of the author's self-lighting speculum for catheterizing the trachea. The speculum is roofed to the distal end, which is curved in a manner to direct the distal end of the catheter forward from the œsophagus and into the larynx and yet it permits of a direct view of the larynx. The battery is enclosed in the handle.

stage of anæsthesia between the excessive respiration occurring when a constant current of air was supplied and the almost entire cessation of efforts at respiration during the periods in which the current of air was regularly interrupted.

The arrangement for automatically interrupting the current of air on these machines, in no way complicates them and is preferable to relying upon the anæsthetist for their production.

It will be noticed that all these machines are open and simple in construction. All parts are easily reached.



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June 13, 1914.*

## FACILITATING THE CRILE METHOD OF TRANSFUSION.

*An Instrument, and Technic for Its Use.*

BY ALFRED KAHN, M. D.,  
New York.

One of the great difficulties, if not the greatest difficulty in making a transfusion by means of the Crile method, is perhaps the cuffing back of the artery over the cannula. Crile threads the artery through the cannula, cuffs it back, and ligates it fast. There is some difficulty in doing this, the artery usually being so small that when it is turned back, it requires the greatest of patience and most careful technic to turn it and ligate. This procedure usually requires several assistants, one to hold the vessel steady, one to hook the vessel and cuff it back, and one to ligate it into position; even then there is always the possibility of the vessel slipping out of position. In order to obviate this, I have invented a little instrument, the cuts of which are herewith shown. Figure 2 shows the instrument, which can be made of any metal, of glass or of wood, or of any material, so long as it follows the contour herein given. The instrument presents, as shown in Fig. 2, the appearance of a very small lead pencil, with a very long point; in other words, it tapers from a dull apex to a base, gradually getting larger (the graduation from apex to base must be long drawn out and very gradual). The reason for this will be appreciated, as we proceed further to illustrate the technic. The instrument is grooved on four sides in four places opposite each other from the apex to the base. Fig. 2, cross section, shows the grooving of the instrument.

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*Kahn: Instrument for Crile Transfusion.*

TECHNIC.

The Crile cannula is threaded on the artery, as usual, then this rod is pushed into the lumen of the

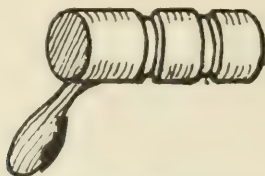


FIG. 1.—The Crile cannula.

vessel, threading the vessel on the instrument. The cannula is then pushed until it catches fast on the rod. This holds cannula and rod fast together, leav-

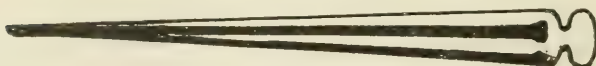


FIG. 2.—Kahn's instrument or rod for facilitating transfusion; a cross section of the instrument is also shown.

ing a small amount of artery beyond the cannula—from one eighth to one fourth inch, or more if de-

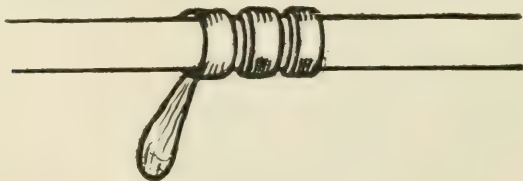


FIG. 3.—Cannula threaded on artery.

sired, of the vessel extending beyond the cannula. This being held fast, it is now a very simple matter



*Kahn: Instrument for Crile Transfusion.*

to pass a hook or small forceps along the grooves in the rod, bite the tip of the artery, and cuff it back over the cannula. If a ligature is tied loosely around this rod, which is about five inches long, it can be brought down over the turned back cuff of artery and ligated over it. This procedure can be

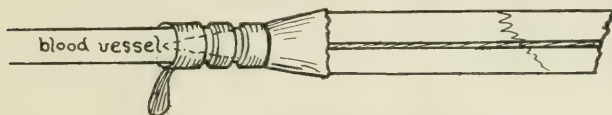


FIG. 4.—Rod introduced into artery.

done by two people and easily—the rod being fastened into the lumen of the vessel makes the handling of the cannula and the vessel quite a simple matter. The grooving of the rod allows the vessel to be cuffed back with ease, making the transfusion

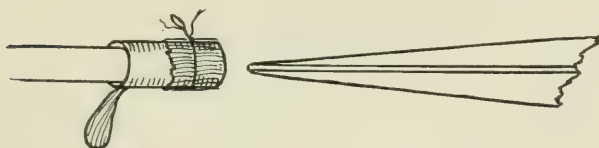


FIG. 5.—Rod withdrawn from lumen of artery, the artery having been cuffed back and tied.

a simple operation. It is now easy to pull your rod out of the vessel's lumen and bring the vein forward over the artery, tying it in place.

34 EAST FORTIETH STREET.



## A MODIFICATION OF THE CRILE CANNULA.

BY ALFRED KAHN, M.D.,

NEW YORK.

To my mind, the Crile cannula is the most simple cannula that we have; but its use has presented difficulties which have caused many suggestions to modify it in certain respects. To me, its most conspicuous defects are its fragility, ease in breaking; and owing to its smallness, the difficulty in handling, and thereby controlling it. Having these two defects in mind, I have endeavored to improve it and have done so in the following way: I have had an instrument made of a hard, bronze, non-tarnishing metal such as is used in the manufacture of many operating knives. This metal is hard to nick or scratch, will not rust, and will stand rough usage.

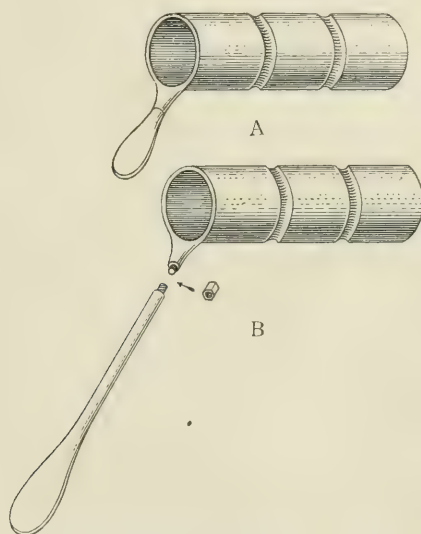


FIG. 1.—A, the Crile cannula with short handle; B, the author's modification, with handle unscrewed showing the lock-nut.

The Crile cannula very often breaks at the junction of its handle portion with the cannula piece. In difficult transfusions where an artery is placed under much tension, in drawing it toward the vein for connection, I have broken many of these cannulæ. I have, therefore, modified the instrument by separating the handle and cannula parts entirely, and this presents many advantages, most important of which is a larger, longer, more solid and firm handle, which allows easy manipulation. The illustration will make the instrument understandable.

After the artery and vein are connected, the rod is unscrewed from the cannula. There is no handle dangling between the vessels; only the little cannula tube. This makes the operation much more clever. There is a small lock-screw between the rod and cannula pieces.



## Notes on surgical pathology in the dog.

By W. HOWARD BARBER and JOHN W. DRAPER.

[From the Laboratory of Surgical Research and from the Department of Pathology, University and Bellevue Hospital Medical College.]

### 1. DIAPHRAGMATIC HERNIA INTO THE PERICARDIAL CAVITY AS CAUSE OF SUDDEN DEATH.

A French poodle, fully grown and bred to extreme fineness, was noticed by his owner, a highly trained observer, to "save himself" in play and for this reason was suspected of having heart-disease. Except for these periods of rest, taken at unexpected and unusual times, the animal appeared physically perfect.

On January 12, 1915, the dog developed general convulsions which lasted one half hour, at the end of which he died. The autopsy, performed the following morning, revealed the following:

1. "*Thorax-Lungs*.—Right slightly congested posterially. Left deeply congested throughout.

"*Heart*.—Pericardial sac large. Right heart compressed by three lobes of liver, gall bladder, and great omentum, 7 by 15 cm. Liver and omentum congested. Gall bladder empty and connected with liver remaining within the abdomen by elongated adhesive band. Deficiency in pericardium measured 3 cm. in diameter and reinforced by fibrous tissue. Deficiency of equal size in central tendon of diaphragm. No hernial sac found.

2. "*Liver*.—Portion within pericardial sac shows extreme passive congestion and fibrosis, indicating that the circulatory obstruction caused by its position has been of long duration. Free portion shows moderate fat infiltration.

"*Edge of Diaphragmatic Opening*.—Appears well rounded and is covered by endothelium,—evidently a congenital defect."

Many phrenic hernias in man have been reported to date.<sup>1</sup>

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<sup>1</sup> Keen's "Surg.," Vol. 4, p. 93.



Grosser and Thoma, alone, have collected 433 cases. Leaming's radiograms of Freeman's case<sup>1</sup> showed ante-mortem practically the entire colon in the chest. It entered the mediastinum in front of the heart curving backward over that organ. The liver was transposed. The hernia was through the right side. Besides the true and the false varieties, there is the analogous condition of eventration of the diaphragm. This is defined,<sup>2</sup> as a dislocation cephalad of the abdominal viscera, particularly of the stomach, on the left side under an abnormally high position of the left vault of the diaphragm. The hernia herewith reported is believed to be a congenital true diaphragmatic one, unique, in that part of the liver as well as the gall bladder and the omentum were found within the pericardial cavity.

Respecting the mechanism of such a hernia,<sup>3</sup> Cunningham says: "The diaphragm is occasionally deficient in the human subject producing hernia either through the central tendon into the pericardial cavity or through the lateral portions of the muscle into the thoracic cavity."<sup>4</sup> Keibel and Mall, describing the developments of the body cavities holds, "In the rabbit the pericardial coelom ends in two dorsal and two ventral recesses, all four of which connect subsequently with the peritoneal coelom. However, only the dorsal recesses break into the peritoneal coelom in the human embryo, and it is this recess or canal which later on encircles the lung and probably forms the main anlage of the pleural coelom."

## 2. BILATERAL NEPHROLITHIASIS AND RIGHT URETERAL CALCULUS.

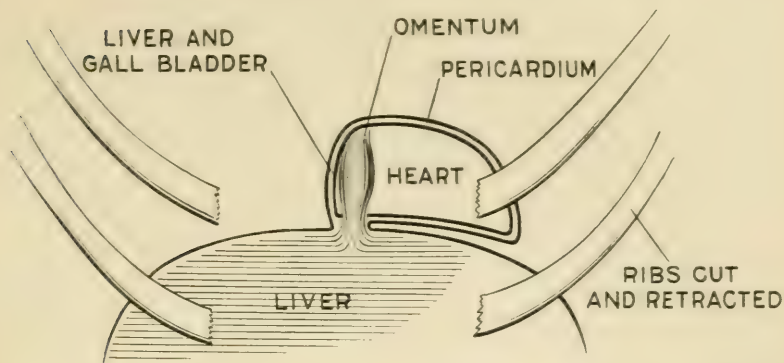
A Dalmatian hound (187 B 2), female, and medium sized had had both ureters transplanted into the sigmoid. The animal lived nine days. At autopsy on the right side a dilated kidney pelvis and a dilated ureter were found. The pelvis contained many small rounded calculi and the ureter a larger elongated stone cephalad to the uretero-colonic anastomosis. On the left side, also, was found a hydronephrosis with a pelvic cast. The ureter on the left side was dilated cephalad only.

<sup>1</sup> Lockwood, Diseases of Stomach, plate XI, p. 406.

<sup>2</sup> Sailer and Rhein, *Am. Jr. Med. Sci.*, Vol. CXXIX, p. 688.

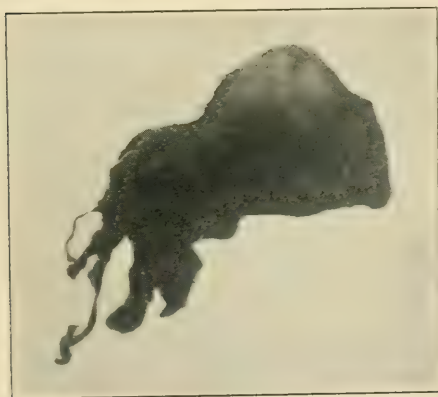
<sup>3</sup> D. J. Cunningham, "Text-Book Anat.," Ed. 2, p. 426.

<sup>4</sup> Keible and Mall, "Human Embryology," Vol. I, p. 526.

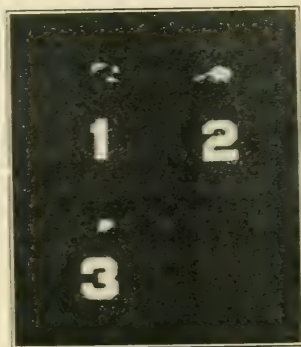


I

DIAGRAM SHOWING HERNIAL OPENING IN DIAPHRAGM AND PERICARDIUM THROUGH WHICH PROTRUDED OMENTUM, LIVER, AND GALL-BLADDER. The right heart was deeply grooved by the liver lobes which had compressed it during growth



2



3

MUSCLE THINNED OUT, LEAVING DELICATE EDGE OF TISSUE FORMING PART OF BORDER OF HERNIAL OPENING IN DIAPHRAGM. Microscopical findings of remaining border: "Edge of *diaphragmatic opening* appears well rounded and is covered by endothelium, evidently a congenital defect."

CALCULI FROM KIDNEYS AND URETER OF DOG WITH TRANSPLANTED URETER: (1) From right pelvis. (2) From left pelvis. (3) From right ureter. ( $\frac{1}{4}$  actual size.)

This selective ureteral dilatation has been noted several times in a series of uretero-sigmoidal transplantations. An attempt has been made to reduce the inevitable resistance at the point of anastomosis to within the physiological limit for the necessarily impaired ureter. When this resistance is too great the first

evidence of physiological strain appears as a dilatation of the cephalad ureter. This dilatation has been noted at varying distances from the kidney pelvis. Other factors being constant, it seems that the length of the hydroureter from the uretero-pelvic junction varies directly with the duration of the terminal overload.

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## GRADUATE SCHOOL

### Research Work in Surgical Pathological Physiology

1915-1916

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## GENERAL ANNOUNCEMENT

New York University announces the admission to the Graduate School of courses in a new department—that of Surgery. It has long been possible to secure credit toward advanced degrees in that School by work in what have been considered the more theoretical branches of the biological sciences; but, until now, the study of surgery has been excluded, for the reason that the emphasis in the past has been placed on the technical rather than on the philosophical side of the science. In response to the recent trend toward the philosophical in surgery, the Graduate School now offers for the first time courses by which it will be possible for the graduate student of surgery to secure the advanced academic degrees of Master and Doctor of Science.

There will be found below short announcements of all the work now offered by the Group of Biological Sciences in the Graduate School of New York University. Special interest, however, is attached to the new course in Surgical Pathological Physiology; and it is thought expedient to give a more complete description of the latter.

This new course in what may be aptly termed biologic surgery will make a special appeal to two classes of students. It will, in the first place, fill the needs of the recent graduate, trained in the hospital and thoroughly versed in technique, who has, however, never had the time or opportunity to think out for himself the fundamental reasons for operating, to differentiate between cause and effect, or, in short, to grasp the application of biologic laws to surgical diagnosis and therapeutics. It will, in the second place, attract a considerable body of students whose interests lie more in the

academic than in the applied side of medicine, and to whom the graduate degrees will be of special value.

The course attempts to suggest rather than teach. It aims, above all, to reflect the tone of recent progress in surgery, which has in the past been characterized by the subordination of technical detail to individual scientific study. It must be thoroughly understood that the course is not suited to those who seek to develop merely the technical and commercial side of their profession; it should, on the other hand, be of fundamental help to practitioners who are looking for the refinement of diagnosis and therapeutics. In this broader sense should lie its greatest appeal.

It is evident, then, that the admission of surgery to the Graduate School carries with it a far greater significance than the mere privilege of granting advanced degrees. It means the emancipation of surgery itself from the academic limitations necessarily circumscribing an ancient and highly technical art; it means the speedy enrollment in its ranks of a higher grade of men than heretofore; it points clearly to more effective and constructive hospital management than has ever before been possible through the work of research fellows and students.

This research course, embracing as it does the broad essential fundamentals of diagnosis and therapeutics, offers, as stated, ample opportunity on the one hand for those wishing to take advanced degrees in surgery, and on the other for surgeons in active practice who may lack both the time and the preliminary degrees necessary to the above but who wish to gain further insight into the philosophical side of their life work. It is not a course in technique, a thorough knowledge of which is essential to those taking it, but rather an inductive course in pragmatic surgery.

#### REQUIREMENTS FOR ADMISSION

Applicants for admission to this course will be of two grades: those having both the B.A. or B.S. and M.D. degrees, and

those holding only the M.D. degree. The latter will receive certificates of proficiency, but no advanced degrees.

Those wishing to secure credit in the Graduate School towards its advanced degrees must submit certificates showing that the candidate is a graduate of a college in good standing, and has received the baccalaureate degree in arts, science, philosophy or letters. The further requirements for the masters' and doctors' degrees will be found explained at length in the complete bulletin of the Graduate School; but, for the new course in surgery they may be briefly defined as follows:

1. The candidate for the master's degree must have completed four courses of 120 hours of laboratory work each, and have submitted a satisfactory thesis.

2. The candidate for the doctor's degree must have a reading knowledge of two modern foreign languages, ordinarily French and German, have completed a minimum requirement of eight courses of 120 hours of laboratory work each, submitted a satisfactory thesis, and passed the required examinations.

A student devoting his full time to the work should ordinarily complete the work for the master's degree in one year; for the doctorate in three.

#### FEES

For each laboratory course of 120 hours, \$25 per year. Laboratory fees are, in general, stated after each course.

#### PLACE

With the exception of the courses in Zoölogy these courses are all held at the University and Bellevue Hospital Medical College, 338 East 26th Street, New York City. The courses in Zoölogy are held at the Biological Laboratory, University Heights.

*For more complete information, address the Registrar, New York University, 32 Waverly Place, New York City.*

## RESEARCH WORK IN SURGICAL PATHOLOGICAL PHYSIOLOGY

*Hours to be arranged*

(No lectures are given by the Department of Surgery  
in Graduate Work)

Courses 3 and 4

### OUTLINE OF TOPICS OFFERED

#### A. ALIMENTARY TRACT

1. The dynamics of the alimentary canal. Dilatation, stricture, ulceration, tetany, atony, autonomic relations.
2. Internal secretions of the duodenum in relation to death from intestinal obstruction, and auto-intoxications.
3. Law of organic compensation in special relation to surgical therapeutics. Ablation, and the post-operative readjustments of the organism. Ileostomy and the vicarious assumption of colonic function. Colectomy. Gastrectomy.

#### B. URINARY TRACT

1. Dynamics of ureter and bladder. Dilatation, stricture, neuro-muscular impairment.
2. Paramount importance of the ureteral prostalsis over the uretero-vesical valve. Hydronephrosis and renal infection.
3. Surgical analogy between the alimentary and urinary neuro-muscular tubes and valves.
4. Uretero-enteric anastomosis based on surgical physiology.

#### C. CEREBRO-SPINAL SYSTEM

1. Hyperthermia in connection with decompression.
2. Experimental studies in increased intradural pressure. (a) Concussion. (b) Contusion, etc. Experimental optic neuritis.
3. Experimental spina bifida.



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## EXCRETORY SYSTEM, CIRCULATORY SYSTEM, CEREBRO-SPINAL SYSTEM

### Courses I and II

1. Estimation of the margin of safety in nephrectomy. Demonstrations of ureteral function and malfunction.
2. Hydronephrosis, etiologically considered.
3. Renal infection, etiologically considered.
4. Pneumonectomy, its margin of safety; mechanisms within the chest provoking death.
5. The thyroid and parathyroids and adrenals.
6. Decompression. Optic neuritis. Experimental demonstration.
7. Experimental spina bifida.
8. Studies in regeneration of bone as demonstrated in the imbrication operation for Pott's Disease.

## PHYSIOLOGICAL SURGERY

### DIGESTIVE SYSTEM

1. Experimental study of the comparative values of the various modern hospital technics, including methods of sterilization, preparation of patient and surgeon.
2. Methods of abdominal incision and closure, experimentally considered.
3. End results of intestinal sutures following different methods and use of different materials. Blood supply, its significance in anastomosis.
4. Experimental study of ulceration from an etiological standpoint. The importance of persistent irritation, traumatic, biochemical and bacterial.
5. Observations following intestinal obstruction: (1) duodenal, (2) ileal, (3) colonic. The significance of feeding intestinal mucosa.
6. Liver.
7. Pancreas.
8. Etiological studies in peritonitis. Absorptive coefficients of serous membranes.

These courses of four hours' laboratory work each week are designed to meet the ends of those students who desire to acquaint themselves with methods of surgical investigation.

The above courses are under the direction of Professor Stewart, and Doctors Draper and Barber.

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**DEPARTMENT OF PHYSIOLOGY**

1. **NUTRITION AND DIET SELECTION.** Lecture course with conferences, open to students with a preliminary knowledge of physiology. This course covers general metabolism in starvation and under protein, carbohydrate and fat ingestion, singly or in combinations to form diets for various conditions. Growth as a physiological function is also discussed. The abnormality of function and dietary treatment of the following pathological conditions are covered: fever, diabetes, tuberculosis, gastro-intestinal disorders, gout, obesity and nephritis.

Two hours a week. Friday, 3.30–5.30. Professor Jackson.

2. **ADVANCED PHYSIOLOGY.** Laboratory Course, open to students with sufficient preliminary work in physiology and chemistry, desiring further work in the more complicated methods of physiological investigation.

Afternoons, 2.00–6.00.

Laboratory fee, \$10.00.

Professor Jackson.

3. **RESEARCH COURSE IN PHYSIOLOGY.** Laboratory work open to students having completed Course 2 or its equivalent. Advanced work in special unsolved problems in physiology.

Time to be arranged.

Laboratory fee, \$20.00.

Professor Jackson.

4. **PATHOLOGICAL PHYSIOLOGY.** Laboratory course open to students who have completed Course 2 or its equivalent. This course will consist in the experimental production by the student of the following abnormalities of function: Heart-valvular lesions, aortic regurgitation and stenosis, venous pulse, extra systoles and heart block. Circulation-blood pressure, hemorrhage and transfusion, hydropericardium, increased intracranial pressure, shock, acapnia, embolism and thrombosis. Endosecretory organs—metabolism and structural changes following, thyroidectomy, parathyroidectomy, pancreatectomy, and adrenalectomy, opotherapy. Thorax-insufflation, pulmonary edema, pneumothorax, hydrothorax, pleuritis. Kidney—acute nephritis, tubular and glomerular.

Saturday, 2.00–6.00 P.M.

Laboratory fee, \$10.00.

Professor Ewing.

**DEPARTMENT OF ANATOMY**

Consultation hours: Professor Senior, daily in the morning, at the Medical College.

201-202. RESEARCH IN ANATOMY. Problems in Vertebrate Embryology. Professor Senior.

203-204. RESEARCH IN HUMAN ANATOMY. Adult and Developmental. Professor Thyng.

**DEPARTMENT OF BACTERIOLOGY AND PUBLIC HEALTH**

Consultation hours: 11 A.M. Saturdays and by appointment.

Each course in this department will require approximately one fourth of the student's entire time for the year or half the student's time for a half year. The lectures and class meetings will be on Saturday mornings at 10 o'clock.

201-202. HYGIENE AND APPLIED BACTERIOLOGY. Course of thirty lectures and thirty hours of laboratory work and thirty hours of practical field work in the city. Full course.

Professor Park and Special Lecturers.

203-204. BACTERIOLOGY. Laboratory exercises and investigations upon acquired immunity. This course will take up the nature of the different anti-bodies, the methods of detecting them and measuring their quantity, and the study of their development and duration in the immunized animals. Full course.

Professor Park and Dr. Noble.

205-206. BACTERIOLOGY. A special study on any important group of bacteria or one bacteriological problem. The subject to be decided upon after consultation. Full course.

Professor Park and Dr. Noble.

**DEPARTMENT OF BIOLOGICAL CHEMISTRY**

Consultation hours: Daily, 9 A.M. to 5 P.M., at the Medical College Laboratory.

201-202. BIOLOGICAL CHEMISTRY, RESEARCH COURSE.

Professor Mandel.

### DEPARTMENT OF PHARMACOLOGY AND APPLIED THERAPEUTICS

Consultation hours: Professor Wallace, daily, at the Medical College.

201-202. PHARMACOLOGY. Research. Special work on assigned subjects. The laboratory is open for this work all day.

Professor Wallace.

203-204. APPLIED THERAPEUTICS. Hospital and Laboratory course, six hours weekly throughout the year. The therapeutic actions of drugs on animals is investigated and their application to patients studied.

Professors Wallace and Brown.

205-206. APPLIED THERAPEUTICS. Research course. Special work, laboratory and clinical, on assigned subjects.

Professors Wallace and Brown.

Those electing Courses 203-204 and 205-206 must have had as a preliminary Course 201-202.

### DEPARTMENT OF ZOÖLOGY

Consultation hours: Professor Bristol at Biological Laboratory, University Heights, by arrangement.

201-202. Comparative Anatomy. (Laboratory Course.)

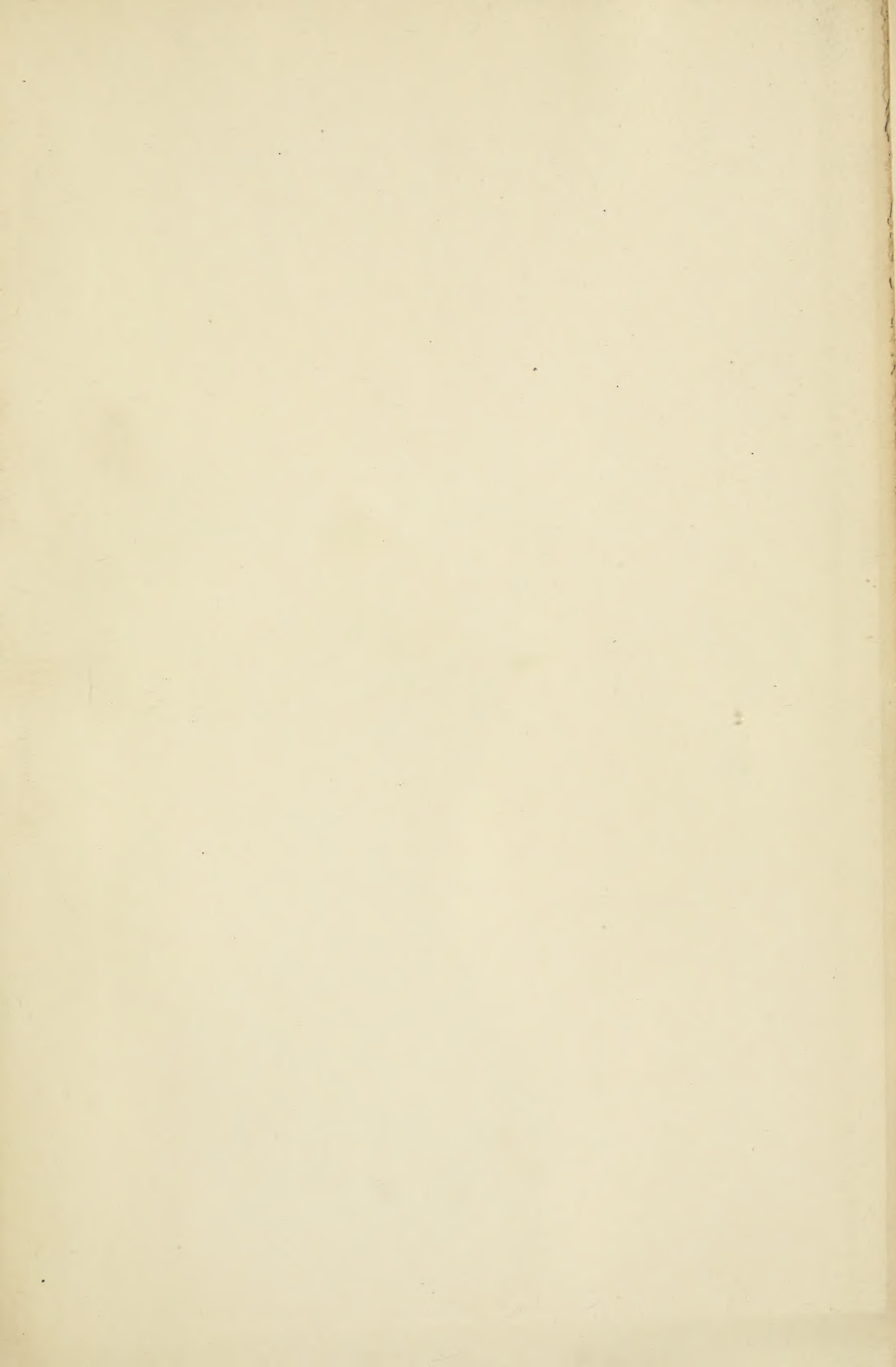
Professor Bristol.

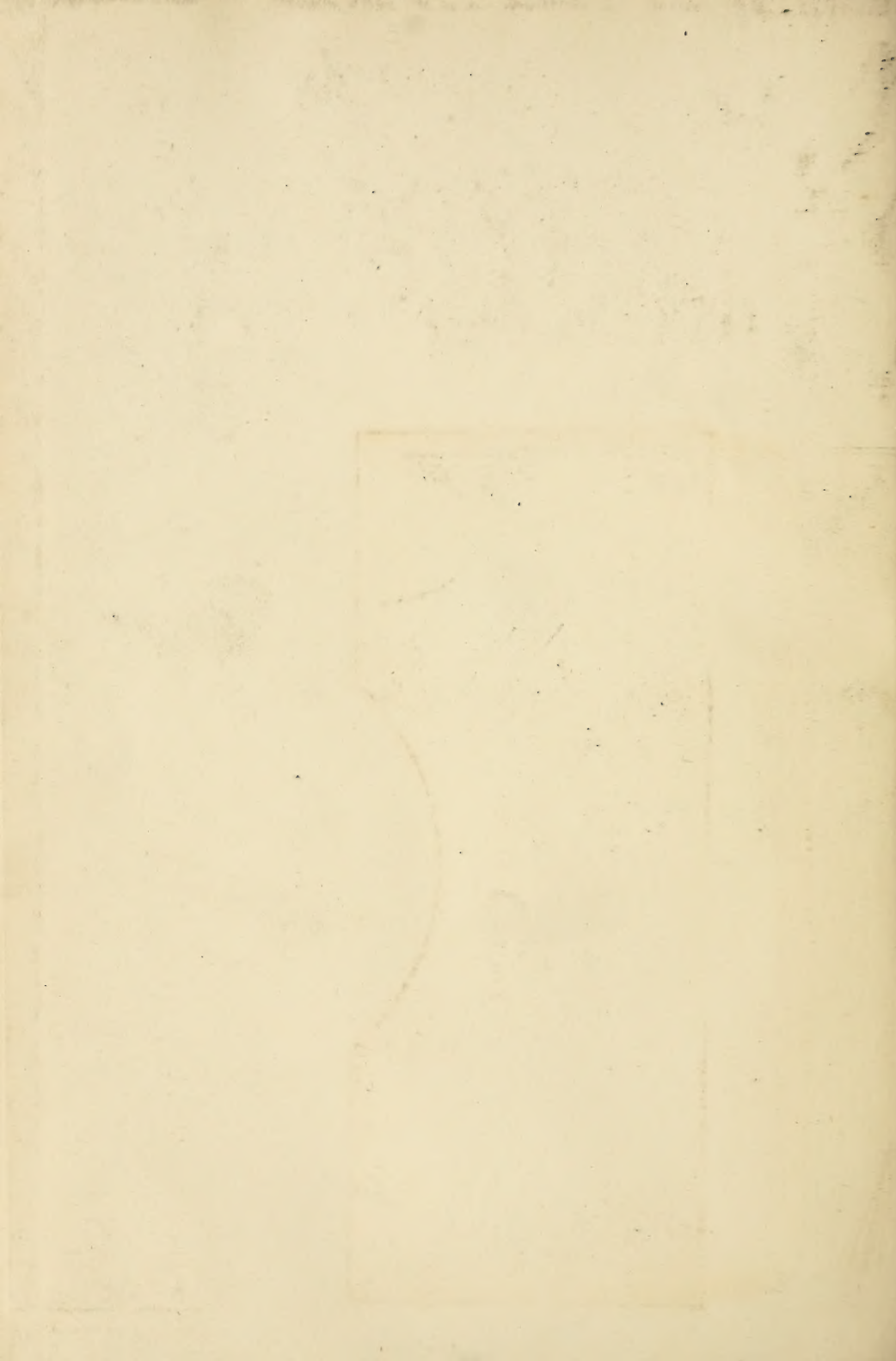
203-204. Research in Zoölogy. (Laboratory Course.)

Professor Bristol.









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